



CLAIM SUPPORT TABLE (CLAIMS 569-1718)
 ENGELHARDT ET AL.
 U.S. PATENT APPLICATION SERIAL NO. 08/486,069
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| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|----------------------------------|--|
| 569 | 329 | Insertion of "detectable" before "labeled nucleic acid fragments" Insertion of "or nucleotide analogs," "which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA," "the sugar analog," "the phosphate analog," and "or the base analog thereof" N.B. FOR SUPPORT IN THE SPECIFICATION, SEE APPLICANTS' MAY 23, 2000 AMENDMENT UNDER 37 C.F.R. §1.115, PAGE 187, LAST ¶ THROUGH PAGE 217, 1ST FULL ¶; SEE PARTICULARLY TABLE "SPECIFICATION REFERENCES TO NUCLEOTIDE ANALOGS" BEGINNING AT BOTTOM OF PAGE 188 AND CONTINUING THROUGH PAGE 191. Insertion of "non-radioactively" after last "detecting" step |
| 570 | | Specification, Page 29, 3rd ¶ ("to determine the presence of a specific deoxyribonucleic acid or ribonucleic acid molecule, . . . derived from a living organism") |
| 571 | | Specification, Page 29, 3rd ¶ ("e.g. bacteria, fungus, virus, yeast, or mammal.") |
| 572 | | <i>ibid.</i> |
| 573 | | Specification, Page 29, 3rd ¶ ("permits diagnosis . . . in a patient") Specification, Page 33, 2nd full ¶ ("In chromosomes from human") |
| 574 | 318 | Specification, Page 29, ("permits diagnosis in a human or other subject"). Note that the base claim for former claim 318 was a detection process and that the base claim for New Claim 574 is a sequencing process. |
| 575 | 319 | Specification, Page 29, 3rd ¶ ("e.g. bacteria, fungus, virus, yeast, or mammal"); See also Page 29, 1st and 4th ¶s for additional support. Note that the base claim for former claim 318 was a detection process and that the base claim for New Claim 574 is a sequencing process. |
| 576 | | Specification, Page 29, 3rd ¶ ("fungus, . . . yeast, or mammal") |
| 577 | | Specification, Page 37, last ¶ through Page 38, 1st ¶ |
| 578 | | Specification, Page 33, 2nd full ¶ ("also works with mammalian chromosomes . . .") |
| 579 | | Same as Claims 577 & 578 above. |
| 580 | | Specification, Page 46, last ¶ through 1st line on Page 47 ("Select from a human gene library some 100 to 200 clones. . . For those clones . . . this determines the location of the cloned DNA on a particular human chromosome.") |
| 581 | | <i>ibid.</i> |
| 582 | | <i>ibid.</i> |
| 583 | 330 | Note the substitution of "or analogs thereof" in place of "dideoxynucleotides". |
| 584 | | Specification, page 12, last ¶ ("The letters x, y, and z represent groups . . . Examples of such nucleotides include . . . 5'-ribonucleoside triphosphates, . . . 5'-deoxyribonucleoside triphosphates, . . .") |
| 585 | 407 | |
| 586 | 335 | |
| 587 | 348 | See Step (B) in Claim 348 ("incorporating said one or more chemically modified nucleotides into said one or more fragments, . . .") |
| 588 | 366 | Claim 366 recites "wherein the labeled oligo- or polynucleotide of interest prepared by said incorporating step comprises at least one terminal modified nucleotide." |
| 589 | | See Specification, Page 25, 2nd ¶ (" . . . the compounds can be prepared by terminal addition to oligo- or polynucleotides to produce compounds in which m or n is 0 depending upon whether the addition is at the 5' or 3' position.") |
| 590 | 336 | With minor language changes |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------------|---|--|
| 591 | | <p>Specification, Page 20, 1st ¶ ("... biotin-labeled RNA probes can be prepared enzymatically using RNA ligase with compounds such as biotinyl-pCp.")</p> <p>Specification, Page 25, 1st two ¶s ("These compounds can be made by enzymatic polymerization of appropriate nucleotides, especially nucleotide triphosphates... Also, the compounds can be prepared by terminal addition to oligo- or polynucleotides to produce compounds in which m or n is 0 depending upon whether the addition is at the 5' or 3' position.")</p> <p>Specification, Page 99, last ¶, through Page 100, last ¶ ("One particularly useful technique... involves the utilization of terminal transferase for the addition of biotinylated dUMP onto the 3' ends of a polypyrimidine or to single-stranded DNA.) SEE ALSO SPECIFICATION, PAGE 99, LAST ¶, LINES 6-8 FROM THE BOTTOM OF THE PAGE. SEE ALSO PAGE, 100, 2ND ¶ ("... BIOTINATED dUTP WAS ADDED TO THE 3' ENDS... EMPLOYING TERMINAL TRANSFERASE... THE RESULTS... ESTABLISHED THAT TERMINAL TRANSFERASE ADDED BIOTINATED dUMP TO THE 3' ENDS.")</p> |
| 592 | | <p>Specification, Page 99, last ¶, through Page 100, last ¶ N.B. TERMINAL TRANSFERASE IS MENTIONED AT LEAST FOUR SEPARATE TIMES). See Claim 591 above. See also Specification, Page 56, Example IV.</p> |
| 593 | | <p>Specification, Page 101, 1st ¶ ("These nucleotides are then incorporated into specific nucleic acids using a DNA or RNA polymerase or ligase reaction or a chemical linkage.")</p> <p>SEE ALSO PAGE 20, 1ST ¶ ("... BIOTIN-LABELED RNA PROBES CAN BE PREPARED ENZYMATICALLY... BY 3' END-LABELING METHODS USING RNA LIGASE WITH COMPOUNDS SUCH AS BIOTINYL-PCP").</p> |
| 594 | | <p>Specification, Page 53, last ¶, through Page 54, 1st two words ("Another technique for tagging nucleic acid material such as DNA or RNA... would be to follow the procedure set forth hereinabove but employing carbodiimide as the cross-linking agent.")</p> <p>Specification, Page 58, Example VII ("Formaldehyde coupling... was carried out...")</p> |
| 595 | | <p>Specification, Page 20, 1st ¶ ("... biotin-labeled probes can be prepared enzymatically... by 3' end-labeling methods using RNA ligase with compounds such as biotinyl-pCp.")</p> <p>Specification, Page 25, 2nd ¶ ("... compounds such as pCp or pUp in which the base is biotinized can be added to existing molecules employing the enzyme RNA ligase.")</p> <p>Specification, Page 60, Example IX ("... T4 DNA ligase...")</p> <p>Specification, Page 77, Example XXXIV ("The lac polyoperator DNA... was ligated, in a blunt end ligation, using T4 ligase, to an adenovirus DNA probe.")</p> <p>Specification, Page 101, 1st ¶ ("These nucleotides are then incorporated into specific nucleic acids using a DNA or RNA polymerase or ligase reaction...")</p> |
| 596 | | <p>Specification, Page 32, 1st ¶ ("DNA probes were nick translated...")</p> <p>Specification, Page 52, 1st ¶ ("Other techniques useful in the practices of this invention include nick translation of DNA employing DNA polymerase...")</p> <p>Specification, Page 67, Example XX ("DNA was labeled with 5-substituted pyrimidine triphosphate by nick translating...")</p> <p>Specification, Page 69, Example XXII ("Phage T4 DNA and phage DNA were labeled by incorporation of H3-deoxyadenosine triphosphate into the DNA by nick translation...")</p> <p>Specification, Page 70, last ¶ ("As previously indicated herein, nick translation is only one of a number of techniques and approaches possible for the production of the modified nucleic acids in accordance with this invention.")</p> <p>Specification, Example XXIII (Lambda DNA was nick translated...")</p> |

| NEW CLAIM NO. | FORMER CLAIM NO. IF APPLICABLE | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|--------------------------------|--|
| 597 | | Specification, Page 25, 1st ¶, line 1 ("These compounds can be made by enzymatic polymerization of appropriate nucleotides, especially nucleotide triphosphates . . .") |
| 598 | | Specification, Page 25, 1st ¶, lines 6-13 ("Illustrative enzymes include DNA polymerase I . . . RNA polymerase . . .") |
| 599 | | <i>ibid.</i> |
| 600 | 331 | Insertion of "nucleotide analogs," "phosphate analog," "sugar analog," & "base analog" in either preamble or nucleotides (i), (ii) and (iii) recited as Markush members Insertion of "non-radioactive" for "Sig is a detectable moiety" |
| 601 | 332 | Insertion of "nucleotide analogs," "purine analog," "7-deazpurine analog," "pyrimidine analog," "sugar analog" Deletion of "Indicator molecule that is self-detecting" from definition of A which now recites "at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal." |
| 602 | 527 | |
| 603 | | Specification, Page 93, lines 9-10 (" . . . wherein P is the phosphoric acid moiety including mono-, di-, tri-, or tetraphosphate, . . .") SEE ALSO SPECIFICATION, PAGE 12, LOWER HALF OF PAGE ("THE LETTERS X, Y, AND Z REPRESENT GROUPS ATTACHED TO THE 5', 3', AND 2' POSITIONS OF THE SUGAR MOIETY. . . MORE LIKELY AT LEAST ONE OF X, Y, AND Z WILL BE A PHOSPHATE-CONTAINING GROUP, EITHER MONO-, DI-, OR TRI-PHOSPHATE . . .") |
| 604 | | Specification, Page 12, last ¶ ("Examples of such nucleotides include 5'-ribonucleoside monophosphates, 5'-ribonucleoside diphosphates, 5'-ribonucleoside triphosphates, 5'-deoxyribonucleoside monophosphates, 5'-deoxyribonucleoside diphosphates, 5'-deoxyribonucleoside triphosphates, 5'-p-ribonucleoside-3'p, and 5'-p-deoxyribonucleoside-3'p.") |
| 605 | | Specification, Page 90, last ¶ ("The special nucleotides of this invention include a phosphoric acid P moiety, a sugar or monosaccharide S moiety, . . .") SEE ALSO SPECIFICATION, PAGE 93, 1ST ¶ (" . . . S the sugar or monosaccharide moiety, . . ."); AND PAGE 103, 2ND ¶ (" . . . the sugar or monosaccharide moiety S, . . ."); SEE ALSO ORIGINALLY FILED CLAIMS 1 & 143 (" . . . S THE SUGAR OR MONOSACCHARIDE MOIETY,") AND 142 (" . . . S THE SUGAR AND MONOSACCHARIDE MOIETY,") |
| 606 | | Specification, Page 2, lower portion Specification, Page 4 (three instances where the furanose ring is shown) Specification, Page 5 (the polynucleotide structure with three furanose rings shown) Specification, Page 8 (a single furanose ring is shown near the middle of the page) Specification, Page 14 (a single furanose ring is depicted) Specification, Page 15 (three furanose ring structures are illustrated) Specification, Page 23 (same as Page 5 above) Specification, Page 62, lines 9-10 ("2-deoxy-3,5-di-O-p-toluy-1-D-ribofuranosyl chloride") Specification, Page 72, lines 8 & 9 from the bottom of the page ("4-amino-5 (tetrazol)-5-yl)-7-(8-D-ribofuranosyl) pyrrolo[2,3-d]pyrimidine") Specification, Page 73, lines 7 & 8 from the bottom of the page ("4-amino-5-cyano-7-(8-D-2-deoxyfuranosyl) pyrrolo[2,3-d]pyrimidine") Specification, Page 92 (two furanose rings are shown in the middle of the page) SEE ALSO APPLICANTS' MAY 1, 1999 FOURTH SUPPLEMENTAL AMENDMENT, PAGE 51 (SECTION 4 MONOSACCHARIDE) THROUGH PAGE 56, 1ST ¶ |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
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| 607 | | Specification, Page 12, last two ¶s ("The letters x, y, and z represent groups attached to the 5', 3', and 2' positions of the sugar moiety. They may be any of H-, HO-, As will be readily appreciated, the most likely identity of z will HO- or H- indicating ribonucleotide or deoxyribonucleotide, respectively. . .") |
| 608 | | Specification, Page 9, last ¶ ("Thus, although purines, pyrimidines and 7-deazapurines are in principal useful, . . .") N.B. THE MARKUSH MEMBERS RECITED IN NEW CLAIM 608 ARE SELECTED FROM THE MARKUSH MEMBERS RECITED IN CLAIM 600. |
| 609 | | N.B. NEW CLAIM 609 RECITES MARKUSH MEMBERS FOR SM AND BASE WHICH ARE TAKEN FROM OTHER CLAIMS. See Claims 605, 606 and 608 above. |
| 610 | 543 | |
| 611 | 544 | |
| 612 | | CLAIM 612 ULTIMATELY DEPENDS FROM CLAIM 606 ("WHEREIN SAID MONOSACCHARIDE COMPRISES A FURANOSE."), CLAIM 605 ("WHEREIN SAID SUGAR MOIETY OR SUGAR ANALOG COMPRISES A MONOSACCHARIDE."), CLAIM 569 (THE INDEPENDENT SEQUENCING PROCESS) AND CLAIM 600 (MARKUSH MEMBERS OF MODIFIED OR LABELED NUCLEOTIDES OR NUCLEOTIDE ANALOGS). THUS, THE ELEMENTS RECITED IN CLAIM 612 ARE TAKEN FROM THESE OTHER PENDING CLAIMS. THE LANGUAGE FOR THE COVALENT ATTACHMENT ("SUCH COVALENT ATTACHMENT DOES NOT SUBSTANTIALLY INTERFERE WITH DOUBLE HELIX FORMATION OR NUCLEIC ACID HYBRIDIZATION") IS ALSO RECITED IN FORMER CLAIM 284 AND PENDING CLAIM 1298. |
| 613 | | Same as Claim 612 above |
| 614 | 310 & 311 | NOTE THAT NEW CLAIM 614 OMITS SIG IN THE STRUCTURAL FORMULA FOR THE COVALENT ATTACHMENT AND ALSO RECITES "NUCLEOTIDE ANALOG." |
| 615 | | Recites elements of other pending dependent claims 604 & 605 ("PM is a mono, di- or tri-phosphate") Specification, Page 57, Example V exemplifies attachment to oligoribonucleotides through the phosphorus or phosphate oxygen |
| 616 | 488 | |
| 617 | | Specification, Page 11, last two ¶s (" . . . It is generally preferred that the chemical linkage include an olefinic bond at the α -position relative to B. . . It is even more preferred that the chemical linkage group be derived from a primary amine, and have the structure $-CH_2-NH- . . .$ ") SEE ALSO ORIGINALLY FILED CLAIM 79 ("WHEREIN SAID CHEMICAL LINKAGE INCLUDES THE MOIETY, $-CH_2-NH- . . .$ ") |
| 618 | | Specification, Page 11, last ¶ ("Examples of preferred linkages derived from allylamine . . .") |
| 619 | | Specification, Page 11, last ¶, through Page 12, 1st ¶. SEE IN PARTICULAR THE STRUCTURAL CHEMICAL FORMULAE AT THE BOTTOM OF PAGE 11. |
| 620 | | Specification, Pages 69-70, Example XXII' ("Binding of Glucosylated DNA to Concanavalin A") and Example XXIII (coupling maltotriose to dUTP). SEE ALSO ORIGINAL CLAIM 160 ("WHEREIN THE B BASE MOIETY OF SAID NUCLEOTIDE IS GLUCOSYLATED."). SEE ALSO ORIGINAL CLAIM 62 ("A POLYNUCLEOTIDE COUPLED OR ATTACHED TO A POLYSACCHARIDE.") |
| 621 | 485 | |
| 622 | 339 | |
| 623 | 340 | |
| 624 | 358 | But note that New Claim 624 depends from a sequencing claim of different scope from former claim 358. |
| 625 | 486 | Note that New Claim 625 recites "covalent attachment" whereas former claim 486 referred to A being attached "directly or through a linkage group." |
| 626 | | Same as Claim 617 above |
| 627 | | Same as Claim 618 above |
| 628 | | Same as Claim 619 above |
| 629 | | Same as Claim 620 above |

| NEW CLAIM NO. | FORMER CLAIM NO. IF APPLICABLE | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|--------------------------------|--|
| 630 | 349 | Note that the base sequencing claim for former claim 349 is different from the base sequencing claim for New Claim 630. |
| 631 | 339 | |
| 632 | 340 | |
| 633 | 358 | Same as Claim 624 above |
| 634 | 410 | |
| 635 | 531 | |
| 636 | 532 | |
| 637 | 533 | |
| 638 | 540 | |
| 639 | 534 | |
| 640 | 542 | |
| 641 | 413 | |
| 642 | 416 | |
| 643 | 419 | |
| 644 | 422 | |
| 645 | 425 | |
| 646 | 428 | |
| 647 | 431 | |
| 648 | 434 | |
| 649 | 437 | |
| 650 | 440 | |
| 651 | 443 | |
| 652 | 446 | |
| 653 | 449 | |
| 654 | 452 | |
| 655 | 458 | |
| 656 | 461 | |
| 657 | 385 | Note that former claim 385 was directed to a chromosomal characterization process, whereas New Claim 657 is directed to a sequencing process. The term "indicator molecule" was also recited in several former dependent claims. See, e.g., former claims 386, 391-392, 401-402 and 404-406. The term "indicator molecule" is also disclosed in Ward et al., U.S. Patents Nos. 4,711,955; 5,328,824; 5,449,767; & 5,476,928. Ward's disclosure is incorporated by reference into the present application. |
| 658 | 385 & 539 | New Claim 658 recites sequence process wherein "said indicator molecule comprises an aromatic compound." Former claim 539, also a sequencing process, recited that "Sig detectable moiety comprises an aromatic . . . group . . ." |
| 659 | | Specification, Page 10, 2nd ¶, through to the end of the page ("A therefore may be any ligand which possesses these properties, . . . Examples of moieties which are useful include: (seven structural formulae depicted including biotin and iminobiotin). Of these the preferred A moieties are biotin and iminobiotin.") Specification, Page 76, Example XXXII ("Fluorescein was coupled to 5-(3-amino-1-propyl)-2'-deoxyuridine-5'-triphosphate (AA-dUTP) . . .") Specification, Page 96, last ¶ ("The Sig moiety could also contain a fluorescing component, such as fluorescein or rhodamine or dansyl.") See also originally filed claims 87-89 & 202-203. |
| 660 | 540 & 542 | New Claim 660 recites "wherein said heterocyclic aromatic compound is fluorescent." Former claims 540 & 542 recited "wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent." |
| 661 | 467 | |
| 662 | 467 | Note that fluorescein is recited as a Markush member in both New Claim 661 and former claim 467. |
| 663 | 464 | |
| 664 | 467 | Same as Claim 661 above |

| NEW CLAIM NO. | FORMER CLAIM NO. IF APPLICABLE | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|--------------------------------|---|
| 665 | 467 | Note that fluorescein is recited as a Markush member in both New Claim 664 and former claim 467. |
| 666 | 470 | |
| 667 | 473 | |
| 668 | 476 | |
| 669 | 479 | |
| 670 | 416 | See New Claim 657 above for support of "indicator molecule." The Markush members of New Claim 670 are taken from former claim 416. |
| 671 | 531 | |
| 672 | 532 | |
| 673 | 533 | |
| 674 | 540 | |
| 675 | 534 | |
| 676 | 542 | |
| 677 | 414 | |
| 678 | 417 | |
| 679 | 420 | |
| 680 | 423 | |
| 681 | 426 | |
| 682 | 429 | |
| 683 | 431 | But note that former claim 431 should have depended from claim 426, not 428. |
| 684 | 435 | |
| 685 | 437 | |
| 686 | 441 | |
| 687 | 444 | |
| 688 | 447 | |
| 689 | 450 | |
| 690 | 453 | |
| 691 | 459 | |
| 692 | 462 | |
| 693 | | See New Claim 657 above for support of "indicator molecule." |
| 694 | 385 & 539 | Same as Claim 658 above |
| 695 | | Same as Claim 659 above |
| 696 | 540 & 542 | Same as Claim 660 above |
| 697 | 468 | |
| 698 | | Same as Claim 697. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 697. |
| 699 | 465 | |
| 700 | 468 | |
| 701 | | Same as Claim 700. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 700. |
| 702 | 471 | |
| 703 | 474 | |
| 704 | 477 | |
| 705 | 480 | Note that former claim 480 should have recited that "A comprises a chelating component" and not "Sig." |
| 706 | | See New Claim 657 above for support of "indicator molecule." The Markush members of New Claim 706 are taken from former claim 417. |
| 707 | 334 | |
| 708 | 368 | Note that former claim 368 recited "wherein said separating step is carried out electrophoretically." New Claim 708 recites "wherein said subjecting step is carried out electrophoretically," the term "subjecting" being reflective of the language in New Claim 569. |

| NEW CLAIM NO. | FORMER CLAIM NO. IF APPLICABLE | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|--------------------------------|---|
| 709 | | <p>Specification, Page 93, lines 18-25 ("... The Sig moiety is covalently attached ... and when so attached is capable of signalling itself or makes itself self-detecting or its presence known ...")</p> <p>Specification, Page 94, lines 7-11 ("The Sig chemical moiety is covalently attached ... and said Sig chemical moiety when attached ... is capable of signalling itself or making itself self-detecting or its presence known ...")</p> <p>Specification, Page 95, lines 10-12 ("... said Sig, when attached to said P moiety being capable of signalling itself or making itself self-detecting or its presence known ...")</p> <p>Specification, Page 95, last five lines ("The resulting nucleotides containing the Sig moiety attached thereto are capable of signalling themselves or making themselves self-detecting or their presence known and being detectable ...")</p> <p>SEE ALSO FORMER CLAIM 369 WHICH RECITED "WHEREIN SAID DETECTING STEP IS CARRIED OUT DIRECTLY" AND DEPENDED FROM FORMER CLAIM 348 (A SEQUENCING CLAIM).</p> |
| 710 | | See New Claim 657 above for support of "indicator molecule." |
| 711 | 371 | Note that former claim 371 recited "said one or more self-indicating nucleotides comprise fluoresceinated nucleotides" and New Claim 711 recites "said one or more indicator molecules comprise fluoresceinated nucleotides or nucleotide analogs." |
| 712 | 372 | Note that former claim 372 recited "said fluoresceinated nucleotides comprise fluoresceinated DNA" and New Claim 712 recites "said fluoresceinated nucleotides or nucleotide analogs comprise fluoresceinated DNA." |
| 713 | 369 | Note that the base claim for former claim 369 was a different sequencing claim from the base sequencing claim for New Claim 713. |
| 714 | 416-417 | New Claim 714 recites Markush elements taken from former claims 416-417. NOTE THAT THE TERMS "A PHOSPHORESCENT COMPOUND" AND "A CHROMOGENIC COMPOUND" ARE RECITED IN NEW CLAIM 717. FOR SUPPORT OF "A CHROMOGENIC COMPOUND," SEE THE SPECIFICATION, PAGES 82-84; SEE IN PARTICULAR, PAGE 82, 1ST ¶ ("... TO CATALYZE A CHROMOGENIC OR FLUOROGENIC REACTION") AND PAGE 84, 1ST ¶ ("... OXIDIZE METHYLENE BLUE TO THE LEUCO FORM IN THE PRESENCE OF MOLECULAR OXYGEN.") |
| 715 | 446 | |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|----------------------------------|--|
| 716 | | <p>For support of "indirectly detectable signal," see the following portions of the Specification:</p> <p>Page 6, Penultimate ¶ ("These various utilities are based upon the ability of the molecules to form stable complexes with polypeptides which in turn can be detected, either by means of properties inherent in the polypeptide or by means of detectable moieties which are attached to, or which interact with, the polypeptide.")</p> <p>Page 7, last three lines, through Page 8, 1st two lines ("... It is preferable that the probe moiety be attached ... so that it can readily interact with antibodies, other detector proteins, or chemical reagents.")</p> <p>Page 25, penultimate ¶, through Page 26, 1st ¶ ("The various modified nucleotides, oligonucleotides, and polynucleotides of this invention may be detected by contacting the compounds with polypeptides ... [which] include one or more moieties which can be detected ... One polypeptide detector for the biotinyl-type probe is avidin. ... If avidin is coupled to potentially demonstrable indicator molecules, ...")</p> <p>Page 26, last ¶, through Page 27, 1st ¶ ("A most preferred protein for biotin-like probe detection is monospecific rabbit IgG, anti-biotin immunoglobulin. ... anti-biotin antibodies have proven extremely useful in detecting specific polynucleotide sequences on chromosomes ...")</p> <p>Page 30, 1st & 2nd ¶ ("... Hybridized nucleic acid duplexes are then identified by forming a complex between the duplex and a suitable polypeptide which carries a detectable moiety. ... can be detected following hybridization with a polynucleotide probe according to this invention based upon complex formation with a suitable detectable polypeptide.")</p> <p>Page 31, last line, through Page 32, 1st line ("... as detected by indirect immunofluorescence for <i>in situ</i> mapping.")</p> <p>Page 33, 1st full ¶ ("indirect immunofluorescence")</p> <p>Page 36, last ¶ ("An alternative to the fluorescence method for visualizing hybridized probes is to direct enzymes such as peroxidase, alkaline phosphatase or (sic) β-galactosidase to the hybridization site where enzymatic conversion of soluble substrates to insoluble colored precipitates permits light microscope visualization.")</p> <p>Page 38, 1st ¶ ("These polynucleotides are hybridized ... and the resulting duplexes contacted with appropriate polypeptides ... [which] include detectable moieties ...")</p> |
| 717 | 416-417 | <p>New Claim 717 recites selected Markush members from former claims 416-417. NOTE THAT "RECEPTOR" IS DESCRIBED IN THE SPECIFICATION, PAGE 102, 1ST ¶ ("3. HORMONE RECEPTORS AND OTHER RECEPTORS ON THE SURFACE OF THE CELL TO WHICH ORGANIC MOLECULES WILL SPECIFICALLY BIND.") NOTE ALSO THAT "LIGAND" RECITED IN NEW CLAIM 717 IS ALSO FOUND IN FORMER CLAIMS 504-505. SEE ALSO SPECIFICATION, PAGE 101, THROUGH PAGE 103, 1ST ¶.</p> |
| 718 | | TO BE ADDRESSED IN A FUTURE RESPONSE |
| 719 | 334 & 416-417 | <p>New Claim 719 recites Markush members directed to seven different detection measurements. Former claim 334 recited "a fluorescent measurement and a chemiluminescent measurement." See also the Specification, Page 37, 1st full ¶ ("... These methods permit the detection of light down to the level of individual photons. With suitable digital processing systems, images can be produced in which each point, i.e. each pixel, of the image is strictly proportional to the number of photons emitted by a point at the object.") Note that light or photon detection is the basis for colorimetric, fluorescent, phosphorescent and chemiluminescent measurements. Further, former claims 416 & 417 recited "an electron density component" and "an enzyme."</p> |
| 720 | 375 | |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS |
|---------------------|---|--|
| | | (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
| 721 | 373 | Insertion of "detectable" before "labeled nucleic acid fragments" Insertion of "or nucleotide analogs," "which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA," "the sugar analog," "the phosphate analog," and "or the base analog thereof" Insertion of "non-radioactively" after last "detecting" step |
| 722 | | Same as Claim 570 above |
| 723 | | Same as Claim 571 above |
| 724 | | Same as Claim 572 above |
| 725 | | Same as Claim 573 above |
| 726 | | Same as Claim 574 above |
| 727 | | Same as Claim 575 above |
| 728 | | Same as Claim 576 above |
| 729 | | Same as Claim 577 above |
| 730 | | Same as Claim 578 above |
| 731 | | Same as Claim 579 above |
| 732 | | Same as Claim 580 above |
| 733 | | Same as Claim 581 above |
| 734 | | Same as Claim 582 above |
| 735 | | Same as Claim 583 above |
| 736 | | Same as Claim 584 above |
| 737 | 407 | Same as Claim 585 above |
| 738 | | Same as Claim 586 above |
| 739 | | Same as Claim 587 above |
| 740 | | Same as Claim 588 above |
| 741 | | Same as Claim 589 above |
| 742 | 336 | Same as Claim 590 above |
| 743 | | Same as Claim 591 above |
| 744 | | Same as Claim 592 above |
| 745 | | Same as Claim 593 above |
| 746 | | Same as Claim 594 above |
| 747 | | Same as Claim 595 above |
| 748 | | Same as Claim 596 above |
| 749 | | Same as Claim 597 above |
| 750 | | Same as Claim 598 above |
| 751 | | <i>ibid.</i> |
| 752 | | Same as Claim 600 above |
| 753 | | Same as Claim 601 above |
| 754 | | Same as Claim 602 above |
| 755 | | Same as Claim 603 above |
| 756 | | Same as Claim 604 above |
| 757 | | Same as Claim 605 above |
| 758 | | Same as Claim 606 above |
| 759 | | Same as Claim 607 above |
| 760 | | Same as Claim 608 above |
| 761 | | See Claim 609 above |
| 762 | 543 | |
| 763 | 544 | |
| 764 | | Same as Claim 612 above |
| 765 | | <i>ibid.</i> |
| 766 | | Same as Claim 614 above |
| 767 | | Same as Claim 615 above |
| 768 | | Same as Claim 616 above |
| 769 | | Same as Claim 617 above |
| 770 | | Same as Claim 618 above |
| 771 | | Same as Claim 619 above |
| 772 | | Same as Claim 620 above |
| 773 | 485 | Same as Claim 621 above |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|----------------------------------|--|
| 774 | 339 | |
| 775 | 340 | |
| 776 | 358 | Same as Claim 624 above |
| 777 | 486 | Same as Claim 625 above |
| 778 | | Same as Claim 617 above |
| 779 | | Same as Claim 618 above |
| 780 | | Same as Claim 619 above |
| 781 | | Same as Claim 620 above |
| 782 | 349 | Same as Claim 630 above |
| 783 | 339 | |
| 784 | 340 | |
| 785 | 358 | Same as Claim 624 above |
| 786 | 410 | Same as Claim 634 above |
| 787 | 531 | |
| 788 | 532 | |
| 789 | 533 | |
| 790 | 540 | Same as Claim 638 above |
| 791 | 534 | |
| 792 | 540 | Same as Claim 638 above |
| 793 | 413 | Same as Claim 641 above |
| 794 | 416 | |
| 795 | 419 | |
| 796 | 422 | |
| 797 | 425 | |
| 798 | 428 | |
| 799 | 431 | |
| 800 | 434 | |
| 801 | 437 | Same as Claim 649 above |
| 802 | 440 | |
| 803 | 443 | |
| 804 | 446 | |
| 805 | 449 | |
| 806 | 452 | |
| 807 | 458 | |
| 808 | 461 | |
| 809 | 385 | Same as Claim 657 above |
| 810 | 385 & 539 | Same as Claim 658 above |
| 811 | | Same as Claim 659 above |
| 812 | 540 & 542 | Same as Claim 660 above |
| 813 | 467 | |
| 814 | | Same as Claim 813 above. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 813. |
| 815 | | Same as Claim 663 above |
| 816 | 467 | Same as Claim 812 above |
| 817 | | Same as Claim 816 above. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 816. |
| 818 | 470 | Same as Claim 666 above |
| 819 | 473 | Same as Claim 667 above |
| 820 | 476 | Same as Claim 668 above |
| 821 | 479 | Same as Claim 669 above |
| 822 | 416 | Same as Claim 670 above |
| 823 | 531 | |
| 824 | 532 | |
| 825 | 533 | |
| 826 | 540 | Same as Claim 638 above. BUT NOTE THAT FORMER CLAIM 540 RECITED "SIG" AND NEW CLAIM 826 RECITES "A." |
| 827 | 534 | |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS |
|---------------------|---|---|
| | | (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
| 828 | 542 | Same as Claim 640 above. BUT NOTE THAT FORMER CLAIM 542 RECITED "SIG" AND NEW CLAIM 828 RECITES "A." |
| 829 | 414 | |
| 830 | 417 | |
| 831 | 420 | |
| 832 | 423 | |
| 833 | 426 | |
| 834 | 429 | |
| 835 | 432 | |
| 836 | 435 | |
| 837 | 438 | |
| 838 | 441 | |
| 839 | 444 | |
| 840 | 447 | |
| 841 | 450 | |
| 842 | 453 | |
| 843 | 459 | |
| 844 | 462 | |
| 845 | 345 | Same as Claim 657 above |
| 846 | 385 & 539 | Same as Claim 658 above |
| 847 | | Same as Claim 659 above |
| 848 | 540 & 542 | Same as Claim 660 above |
| 849 | 468 | |
| 850 | | Same as Claim 849 above. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 849. |
| 851 | 465 | |
| 852 | 468 | Same as Claim 848 above |
| 853 | | Same as Claim 852 above. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 852. |
| 854 | 471 | |
| 855 | 474 | Same as Claim 703 above |
| 856 | 477 | Same as Claim 704 above |
| 857 | 480 | Same as Claim 705 above. BUT NOTE THAT FORMER CLAIM 480 SHOULD HAVE RECITED "A" AND NOT "SIG." |
| 858 | 417 | Same as Claim 706 above |
| 859 | 334 | Same as Claim 707 above |
| 860 | 368 | Note that former claim 368 recited "wherein said separating step is carried out electrophoretically." New Claim 860 recites "wherein said separating or resolving step is carried out electrophoretically," the term "resolving" being reflective of the language in New Claim 721. |
| 861 | | Same as Claim 709 above |
| 862 | | Same as New Claim 710 above. See New Claim 657 above for support of "indicator molecule." |
| 863 | | Same as Claim 711 above |
| 864 | | Same as Claim 712 above |
| 865 | | Same as Claim 713 above |
| 866 | 416-417 | Same as Claim 714 above. NOTE THAT THE BASE SEQUENCING CLAIM FOR CLAIM 866 IS DIFFERENT FROM THE BASE SEQUENCING CLAIMS FOR CLAIM 714. |
| 867 | 446 | Same as Claim 715 above |
| 868 | | Same as Claim 716 above |
| 869 | 416-417 | Same as Claim 717 above |
| 870 | | TO BE ADDRESSED IN A FUTURE RESPONSE |
| 871 | 334 & 416-417 | Same as Claim 719 above |
| 872 | 374 | |

| NEW CLAIM NO. | FORMER CLAIM NO. IF APPLICABLE | COMMENTS |
|---------------------|---|---|
| | | (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
| 873 | 520 | Insertion of "detectable" before "labeled nucleic acid fragments" Insertion of "or nucleotide analogs," "which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA," "the sugar analog," "the phosphate analog," and "or the base analog thereof" Changed "within" to "with" in second step ("detecting") Insertion of "non-radioactively" after second step ("detecting") |
| 874 | | Same as Claim 570 above |
| 875 | | Same as Claim 571 above |
| 876 | | Same as Claim 572 above |
| 877 | | Same as Claim 573 above |
| 878 | | Same as Claim 574 above |
| 879 | | Same as Claim 575 above |
| 880 | | Same as Claim 576 above |
| 881 | | Same as Claim 577 above |
| 882 | | Same as Claim 578 above |
| 883 | | Same as Claim 579 above |
| 884 | | Same as Claim 580 above |
| 885 | | Same as Claim 581 above |
| 886 | | Same as Claim 582 above |
| 887 | | Same as Claim 583 above |
| 888 | | Same as Claim 584 above |
| 889 | 407 | But note that New Claim 889 depends from a different independent sequencing claim. |
| 890 | | Same as Claim 586 above |
| 891 | | Same as Claim 587 above |
| 892 | | Same as Claim 588 above |
| 893 | | Same as Claim 589 above |
| 894 | 336 | Same as Claim 590 above |
| 895 | | Same as Claim 591 above |
| 896 | | Same as Claim 592 above |
| 897 | | Same as Claim 593 above |
| 898 | | Same as Claim 594 above |
| 899 | | Same as Claim 595 above |
| 900 | | Same as Claim 596 above |
| 901 | | Same as Claim 597 above |
| 902 | | Same as Claim 598 above |
| 903 | | <i>ibid.</i> |
| 904 | 522 | Insertion of "nucleotide analogs," "phosphate analog," "sugar analog," & "base analog" in either preamble or nucleotides (i), (ii) and (iii) recited as Markush members Insertion of "non-radioactive" for "Sig is a detectable moiety" |
| 905 | 524 | Insertion of "nucleotide analogs," "purine analog," "7-deazpurine analog," "pyrimidine analog," "sugar analog" Deletion of "indicator molecule that is self-detecting" from definition of A which now recites "at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal." |
| 906 | | Same as Claim 602 above |
| 907 | | Same as Claim 603 above |
| 908 | | Same as Claim 604 above |
| 909 | | Same as Claim 605 above |
| 910 | | Same as Claim 606 above |
| 911 | | Same as Claim 607 above |
| 912 | | Same as Claim 608 above |
| 913 | | See Claim 609 above |
| 914 | 567 | |
| 915 | 568 | |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|----------------------------------|---|
| 916 | | Same as Claim 612 above |
| 917 | | <i>ibid.</i> |
| 918 | | Same as Claim 614 above |
| 919 | | Same as Claim 615 above |
| 920 | | Same as Claim 616 above |
| 921 | | Same as Claim 617 above |
| 922 | | Same as Claim 618 above |
| 923 | | Same as Claim 619 above |
| 924 | | Same as Claim 620 above |
| 925 | 485 | Same as Claim 621 above |
| 926 | 339 | |
| 927 | 340 | |
| 928 | 358 | Same as Claim 624 above |
| 929 | 486 | Same as Claim 625 above |
| 930 | | Same as Claim 617 above |
| 931 | | Same as Claim 618 above |
| 932 | | Same as Claim 619 above |
| 933 | | Same as Claim 620 above |
| 934 | 349 | Same as Claim 630 above |
| 935 | 339 | |
| 936 | 340 | |
| 937 | 358 | Same as Claim 624 above |
| 938 | 410 | Same as Claim 634 above. Note that New Claim 938 depends from a different sequencing claim than Claim 634. |
| 939 | 531 | |
| 940 | 532 | |
| 941 | 533 | |
| 942 | 564 | |
| 943 | 534 | |
| 944 | 566 | |
| 945 | 413 | Same as Claim 641 above. NOTE THAT NEW CLAIM 945 DEPENDS FROM A DIFFERENT SEQUENCING PROCESS FROM THAT OF FORMER CLAIM 413. |
| 946 | 416 | Same as Claim 642 above. NOTE THAT NEW CLAIM 946 DEPENDS FROM A DIFFERENT SEQUENCING PROCESS FROM THAT OF FORMER CLAIM 416. |
| 947 | 419 | Same as Claim 643 above. NOTE THAT NEW CLAIM 947 DEPENDS FROM A DIFFERENT SEQUENCING PROCESS FROM THAT OF FORMER CLAIM 419. |
| 948 | 422 | Same as Claim 644 above. NOTE THAT NEW CLAIM 948 DEPENDS FROM A DIFFERENT SEQUENCING PROCESS FROM THAT OF FORMER CLAIM 422. |
| 949 | 425 | Same as Claim 645 above. NOTE THAT NEW CLAIM 949 DEPENDS FROM A DIFFERENT SEQUENCING PROCESS FROM THAT OF FORMER CLAIM 425. |
| 950 | 428 | Same as Claim 646 above. NOTE THAT NEW CLAIM 950 DEPENDS FROM A DIFFERENT SEQUENCING PROCESS FROM THAT OF FORMER CLAIM 428. |
| 951 | 431 | Same as Claim 647 above. NOTE THAT NEW CLAIM 951 DEPENDS FROM A DIFFERENT SEQUENCING PROCESS FROM THAT OF FORMER CLAIM 431. |
| 952 | 434 | Same as Claim 648 above. NOTE THAT NEW CLAIM 952 DEPENDS FROM A DIFFERENT SEQUENCING PROCESS FROM THAT OF FORMER CLAIM 434. |
| 953 | 437 | Same as Claim 649 BUT NOTE THAT NEW CLAIM 953 DEPENDS FROM A DIFFERENT BASE SEQUENCING CLAIM FROM THAT OF FORMER CLAIM 437. |
| 954 | 440 | Same as Claim 650 BUT NOTE THAT NEW CLAIM 954 DEPENDS FROM A DIFFERENT BASE SEQUENCING CLAIM FROM THAT OF FORMER CLAIM 440. |
| 955 | 443 | Same as Claim 651 BUT NOTE THAT NEW CLAIM 954 DEPENDS FROM A DIFFERENT BASE SEQUENCING CLAIM FROM THAT OF FORMER CLAIM 443. |
| 956 | 446 | Same as Claim 652 BUT NOTE THAT NEW CLAIM 954 DEPENDS FROM A DIFFERENT BASE SEQUENCING CLAIM FROM THAT OF FORMER CLAIM 446. |
| 957 | 449 | Same as Claim 653 BUT NOTE THAT NEW CLAIM 954 DEPENDS FROM A DIFFERENT BASE SEQUENCING CLAIM FROM THAT OF FORMER CLAIM 449. |
| 958 | 452 | Same as Claim 654 BUT NOTE THAT NEW CLAIM 954 DEPENDS FROM A DIFFERENT BASE SEQUENCING CLAIM FROM THAT OF FORMER CLAIM 452. |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS |
|---------------------|---|---|
| | | (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
| 959 | 455 | Same as Claim 655 BUT NOTE THAT NEW CLAIM 954 DEPENDS FROM A DIFFERENT BASE SEQUENCING CLAIM FROM THAT OF FORMER CLAIM 455. |
| 960 | 458 | Same as Claim 656 BUT NOTE THAT NEW CLAIM 954 DEPENDS FROM A DIFFERENT BASE SEQUENCING CLAIM FROM THAT OF FORMER CLAIM 458. |
| 961 | 385 | Same as Claim 657 above |
| 962 | 385 & 539 | Same as Claim 658 above |
| 963 | | Same as Claim 659 above |
| 964 | 564 & 566 | New Claim 964 recites "wherein said heterocyclic aromatic compound is fluorescent." Former claims 540 & 542 recited "wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent." |
| 965 | 467 | Same as Claim 661 above BUT NOTE THAT THE BASE SEQUENCING CLAIMS FOR CLAIMS 467 AND 965 ARE DIFFERENT. |
| 966 | | Same as Claim 965 above. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 965. |
| 967 | | Same as Claim 663 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 663 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 967. |
| 968 | 467 | Same as Claim 965 above |
| 969 | | Same as Claim 968 above. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 968. |
| 970 | | Same as Claim 666 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 666 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 970. |
| 971 | 473 | Same as Claim 667 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 667 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 971. |
| 972 | 476 | Same as Claim 668 above BUT NOTE THE BASE SEQUENCING CLAIM FOR NEW CLAIM 668 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 972. |
| 973 | 479 | Same as Claim 669 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 669 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 973. |
| 974 | | Same as Claim 670 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 670 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 974. |
| 975 | 531 | |
| 976 | 532 | |
| 977 | 533 | |
| 978 | 564 | But note that former claim 564 ultimately recited "Sig" and New Claim 978 ultimately recites "A." |
| 979 | 534 | |
| 980 | 566 | But note that former claim 566 recited "Sig" and New Claim 980 ultimately recites "A." |
| 981 | 414 | Same as Claim 677 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 981 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 677. |
| 982 | 417 | Same as Claim 678 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 982 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 678. |
| 983 | 420 | Same as Claim 679 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 983 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 679. |
| 984 | 423 | Same as Claim 680 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 984 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 680. |
| 985 | 426 | Same as Claim 681 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 985 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 681. |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS |
|---------------------|---|---|
| | | (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
| 986 | 429 | Same as Claim 682 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 986 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 682. |
| 987 | 432 | Same as Claim 683 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 987 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 683. |
| 988 | 435 | Note that New Claim 988 depends from a different sequencing process from that of former claim 435. |
| 989 | 438 | Same as Claim 685 above BUT NOTE THAT THE BASE SEQUENCING CLAIMS FOR CLAIMS 685 AND 989 ARE DIFFERENT. |
| 990 | 441 | Same as Claim 686 above BUT NOTE THAT THE BASE SEQUENCING CLAIMS FOR CLAIMS 686 AND 990 ARE DIFFERENT. |
| 991 | 444 | Same as Claim 687 above BUT NOTE THAT THE BASE SEQUENCING CLAIMS FOR CLAIMS 687 AND 991 ARE DIFFERENT. |
| 992 | 447 | Same as Claim 688 above BUT NOTE THAT THE BASE SEQUENCING CLAIMS FOR CLAIMS 688 AND 992 ARE DIFFERENT. |
| 993 | 450 | Same as Claim 689 above BUT NOTE THAT THE BASE SEQUENCING CLAIMS FOR CLAIMS 689 AND 993 ARE DIFFERENT. |
| 994 | 453 | Same as Claim 690 above BUT NOTE THAT THE BASE SEQUENCING CLAIMS FOR CLAIMS 690 AND 994 ARE DIFFERENT. |
| 995 | 459 | Same as Claim 691 above BUT NOTE THAT THE BASE SEQUENCING CLAIMS FOR CLAIMS 691 AND 995 ARE DIFFERENT. |
| 996 | 462 | Same as Claim 692 above BUT NOTE THAT THE BASE SEQUENCING CLAIMS FOR CLAIMS 692 AND 996 ARE DIFFERENT. |
| 997 | 385 | Same as Claim 657 above |
| 998 | 385 & 539 | Same as Claim 658 above |
| 999 | | Same as Claim 659 above |
| 1000 | 564 & 566 | Same as Claim 964 above |
| 1001 | 468 | Same as Claim 697 above BUT NOTE THAT THE BASE SEQUENCING CLAIMS FOR CLAIMS 468 AND 1001 ARE DIFFERENT. |
| 1002 | | Same as Claim 1001 above. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 1001. |
| 1003 | 465 | Same as Claim 699 above. BUT NOTE THAT THE BASE SEQUENCING CLAIMS FOR CLAIMS 699 AND 1003 ARE DIFFERENT. |
| 1004 | 468 | Same as Claim 1001 above |
| 1005 | | Same as Claim 1004 above. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 1004. |
| 1006 | 471 | Same as Claim 702 above. BUT NOTE THAT THE BASE SEQUENCING CLAIMS FOR CLAIMS 702 AND 1006 ARE DIFFERENT. |
| 1007 | 474 | Same as Claim 703 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 703 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1007. |
| 1008 | 477 | Same as Claim 704 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 704 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1008. |
| 1009 | 480 | Same as Claim 705 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 705 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1009. ALSO, FORMER CLAIM 480 SHOULD HAVE RECITED "A" AND NOT "SIG." |
| 1010 | | Same as Claim 706 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 706 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1010. |
| 1011 | | Same as Claim 707 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 707 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1011. |
| 1012 | 368 | NOTE THAT FORMER CLAIM 369 RECITED "WHEREIN SAID SEPARATING STEP IS CARRIED OUT ELECTROPHORETICALLY." |
| 1013 | | Same as Claim 709 above |
| 1014 | | See New Claim 657 above for support of "indicator molecule." |

| NEW CLAIM NO. | FORMER CLAIM NO. IF APPLICABLE | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|--------------------------------|--|
| 1015 | 371 | Note that former claim 371 recited "said one or more self-indicating nucleotides comprise fluoresceinated nucleotides" and New Claim 1015 recites "said one or more indicator molecules comprise fluoresceinated nucleotides or nucleotide analogs." |
| 1016 | 372 | Note that former claim 372 recited "said fluoresceinated nucleotides comprise fluoresceinated DNA" and New Claim 1016 recites "said fluoresceinated nucleotides or nucleotide analogs comprise fluoresceinated DNA." |
| 1017 | 369 | Note that the base claim for former claim 369 was a different sequencing claim from the base sequencing claim for New Claim 1017. |
| 1018 | 416-417 | Same as Claim 714 above. NOTE THAT THE BASE SEQUENCING CLAIM FOR CLAIM 1018 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR CLAIM 714. |
| 1019 | 446 | Same as Claim 715 above. NOTE THAT THE BASE SEQUENCING CLAIM FOR CLAIM 1019 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR CLAIM 715. |
| 1020 | | Same as Claim 716 above |
| 1021 | 416-417 | Same as Claim 717 above. BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR CLAIM 1021 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR CLAIM 717. |
| 1022 | | TO BE ADDRESSED IN A FUTURE RESPONSE |
| 1023 | 334 & 416-417 | Same as Claim 719 above. NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 719 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1023. |
| 1024 | 525 | |
| 1025 | 521 | Insertion of "detectable" before "labeled nucleic acid fragments" Insertion of "or nucleotide analogs," "which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA," "the sugar analog," "the phosphate analog," and "or the base analog thereof" |
| 1026 | | Same as Claim 570 above |
| 1027 | | Same as Claim 571 above |
| 1028 | | Same as Claim 572 above |
| 1029 | | Same as Claim 573 above |
| 1030 | | Same as Claim 574 above |
| 1031 | | Same as Claim 575 above |
| 1032 | | Same as Claim 576 above |
| 1033 | | Same as Claim 577 above |
| 1034 | | Same as Claim 578 above |
| 1035 | | Same as Claim 579 above |
| 1036 | | Same as Claim 580 above |
| 1037 | | Same as Claim 581 above |
| 1038 | | Same as Claim 582 above |
| 1039 | | Same as Claim 583 above |
| 1040 | | Same as Claim 584 above |
| 1041 | 407 | But New Claim 1041 depends from a different independent sequencing claim than that from New Claim 407 depends. |
| 1042 | | Same as Claim 586 above |
| 1043 | | Same as Claim 587 |
| 1044 | | Same as Claim 588 |
| 1045 | | Same as Claim 589 |
| 1046 | | Same as Claim 590 |
| 1047 | | Same as Claim 591 |
| 1048 | | Same as Claim 592 above |
| 1049 | | Same as Claim 593 above |
| 1050 | | Same as Claim 594 above |
| 1051 | | Same as Claim 595 above |
| 1052 | | Same as Claim 596 above |
| 1053 | | Same as Claim 597 above |
| 1054 | | Same as Claim 598 above |

| NEW CLAIM NO. | FORMER CLAIM NO. IF APPLICABLE | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|--------------------------------|--|
| 1055 | | <i>ibid.</i> |
| 1056 | 522 | Insertion of "nucleotide analogs," "phosphate analog," "sugar analog," & "base analog" in either preamble or nucleotides (i), (ii) and (iii) recited as Markush members Insertion of "non-radioactive" for "Sig is a detectable moiety" |
| 1057 | 524 | Insertion of "nucleotide analogs," "purine analog," "7-deazapurine analog," "pyrimidine analog", "sugar analog" Deletion of "indicator molecule that is self-detecting" from definition of A which now recites "at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal." |
| 1058 | | Same as Claim 602 above |
| 1059 | | Same as Claim 603 above |
| 1060 | | Same as Claim 604 above |
| 1061 | | Same as Claim 605 above |
| 1062 | | Same as Claim 606 above |
| 1063 | | Same as Claim 607 above |
| 1064 | | Same as Claim 608 above |
| 1065 | | See Claim 609 above |
| 1066 | 567 | |
| 1067 | 568 | |
| 1068 | | Same as Claim 612 above |
| 1069 | | <i>ibid.</i> |
| 1070 | | Same as Claim 614 above |
| 1071 | | Same as Claim 615 above |
| 1072 | | Same as Claim 616 above |
| 1073 | | Same as Claim 617 above |
| 1074 | | Same as Claim 618 above |
| 1075 | | Same as Claim 619 above |
| 1076 | | Same as Claim 620 above |
| 1077 | 485 | Same as Claim 621 above |
| 1078 | 339 | |
| 1079 | 340 | |
| 1080 | 358 | Same as Claim 624 |
| 1081 | 486 | Same as Claim 625 above |
| 1082 | | Same as Claim 617 above |
| 1083 | | Same as Claim 618 above |
| 1084 | | Same as Claim 619 above |
| 1085 | | Same as Claim 620 above |
| 1086 | 349 | Same as Claim 630 above |
| 1087 | 339 | |
| 1088 | 340 | |
| 1089 | 358 | Same as Claim 624 above |
| 1090 | 410 | Same as Claim 938 above |
| 1091 | 531 | |
| 1092 | 532 | |
| 1093 | 533 | |
| 1094 | 564 | Same as Claim 942 above |
| 1095 | 534 | |
| 1096 | 566 | Same as Claim 944 above |
| 1097 | 413 | Same as Claim 945 above |
| 1098 | 416 | Same as Claim 642 above. NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 642 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1098. |
| 1099 | 419 | Same as Claim 643 above. NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 643 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1099. |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|----------------------------------|---|
| 1100 | 422 | Same as Claim 644 above. NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 644 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1100. |
| 1101 | 425 | Same as Claim 645 above. NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 645 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1101. |
| 1102 | 428 | Same as Claim 646 above. NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 646 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1102. |
| 1103 | 431 | Same as Claim 647 above. NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 647 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1103. |
| 1104 | 434 | Same as Claim 648 above. NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 648 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1104. |
| 1105 | 437 | Same as Claim 649 above. NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 649 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1105. |
| 1106 | 440 | Same as Claim 650 above. NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 650 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1106. |
| 1107 | 443 | Same as Claim 651 above. NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 651 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1107. |
| 1108 | 446 | Same as Claim 652 above. NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 652 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1108. |
| 1109 | 449 | Same as Claim 653 above. NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 653 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1109. |
| 1110 | 452 | Same as Claim 654 above. NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 654 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1110. |
| 1111 | 458 | Same as Claim 655 above. NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 655 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1111. |
| 1112 | 461 | Same as Claim 656 above. NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 656 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1112. |
| 1113 | 385 | Same as Claim 657 above |
| 1114 | 385 & 539 | Same as Claim 658 above |
| 1115 | | Same as Claim 659 above |
| 1116 | 564 & 566 | Same as Claim 964 except that the base sequencing claim is different. |
| 1117 | 467 | Same as Claim 965 above BUT NOTE THAT THE BASE SEQUENCING CLAIMS FOR CLAIMS 467 AND 1117 ARE ALSO DIFFERENT. |
| 1118 | | Same as Claim 1117 above. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 1117. |
| 1119 | | Same as Claim 663 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 663 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1119. |
| 1120 | 467 | Same as Claim 1117 above |
| 1121 | | Same as Claim 1120 above. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 1120. |
| 1122 | | Same as Claim 666 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 666 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1122. |
| 1123 | | Same as Claim 971 above |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS |
|---------------------|---|---|
| | | (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
| 1124 | 476 | Same as Claim 668 above BUT NOTE THE BASE SEQUENCING CLAIM FOR NEW CLAIM 668 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1124. |
| 1125 | 479 | Same as Claim 669 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 669 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1125. |
| 1126 | | Same as Claim 670 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 670 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1126. |
| 1127 | 531 | |
| 1128 | 532 | |
| 1129 | 533 | |
| 1130 | 564 | But note that former claim 564 recited "Sig" and New Claim 1130 ultimately recites "A." |
| 1131 | 534 | |
| 1132 | 566 | But note that former claim 566 recited "Sig" and New Claim 1132 ultimately recites "A." |
| 1133 | 414 | Same as Claim 677 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 677 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1133. |
| 1134 | 417 | Same as Claim 678 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 678 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1134. |
| 1135 | 420 | Same as Claim 679 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 679 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1135. |
| 1136 | 423 | Same as Claim 680 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 680 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1136. |
| 1137 | 426 | Same as Claim 681 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 681 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1137. |
| 1138 | 429 | Same as Claim 682 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 682 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1138. |
| 1139 | 432 | Same as Claim 683 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 683 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1139. |
| 1140 | 435 | Same as Claim 684 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 684 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1140. |
| 1141 | 438 | Same as Claim 685 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 685 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1141. |
| 1142 | 441 | Same as Claim 686 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 686 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1142. |
| 1143 | 444 | Same as Claim 687 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 687 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1143. |
| 1144 | 447 | Same as Claim 688 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 688 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1144. |
| 1145 | 450 | Same as Claim 689 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 689 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1145. |
| 1146 | 453 | Same as Claim 690 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 690 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1146. |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|----------------------------------|---|
| 1147 | 459 | Same as Claim 691 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 691 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1147. |
| 1148 | 462 | Same as Claim 692 BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 692 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1141. |
| 1149 | | See New Claim 657 above for support of "Indicator molecule." |
| 1150 | 385 & 539 | Same as Claim 658 above |
| 1151 | | Same as Claim 659 above |
| 1152 | 564 & 566 | Same as Claim 1116 above |
| 1153 | 468 | Same as Claim 1001 above BUT NOTE THAT THE BASE SEQUENCING CLAIMS FOR CLAIMS 468 AND 1153 ARE DIFFERENT. |
| 1154 | | Same as Claim 1153 above. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 1153. |
| 1155 | | Same as Claim 699 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR CLAIM 699 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR 1155. |
| 1156 | 468 | Same as Claim 1153 above |
| 1157 | | Same as Claim 1156 above. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 1156. |
| 1158 | | Same as Claim 702 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 702 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1158. |
| 1159 | | Same as Claim 1007 above |
| 1160 | | Same as Claim 704 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 704 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1160. |
| 1161 | | Same as Claim 705 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 705 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1161. |
| 1162 | | Same as Claim 706 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 706 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1162. |
| 1163 | | Same as Claim 707 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 707 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1163. |
| 1164 | | Same as Claim 708 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 708 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1164. |
| 1165 | | Same as Claim 709 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 709 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1165. |
| 1166 | | Same as Claim 710 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 710 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1166. |
| 1167 | | Same as Claim 711 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 711 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1167. |
| 1168 | | Same as Claim 712 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 712 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1168. |
| 1169 | | Same as Claim 713 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 713 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1169. |
| 1170 | 416-417 | Same as Claim 714 above. NOTE THAT THE BASE SEQUENCING CLAIM FOR CLAIM 1170 IS DIFFERENT FROM THE BASE SEQUENCING CLAIMS FOR CLAIM 714. |
| 1171 | 446 | Same as Claim 715 above. NOTE THAT THE BASE SEQUENCING CLAIM FOR CLAIM 1171 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR CLAIM 715. |
| 1172 | | Same as Claim 716 above. |

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Filed: June 7, 1995

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| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|----------------------------------|--|
| 1173 | 416-417 | Same as Claim 717 above. BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR CLAIM 1173 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR CLAIM 717. |
| 1174 | | TO BE ADDRESSED IN A FUTURE RESPONSE |
| 1175 | 334 & 416-417 | Same as Claim 719 above. NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 719 IS DIFFERENT FROM THE BASE SEQUENCING CLAIM FOR NEW CLAIM 1175. |
| 1176 | 525 | NOTE THAT CLAIM 525 DEPENDED FROM FORMER CLAIM 520. CLAIM 1176 IS SIMILAR IN SCOPE AND LANGUAGE TO FORMER CLAIM 521. ALSO, THE TERM "SELF-INDICATING" IS ABSENT IN NEW CLAIM 1176. |
| 1177 | 348 | <p>Substitution of new components (i), (ii) and (iii) in providing step (A)</p> <p>Insertion of "detectable" before "chemically modified or labeled nucleotides . . ."</p> <p>Insertion in providing step (A) of "or nucleotide analogs," "which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA," "the sugar analog," "the phosphate analog," and "or the base analog thereof" N.B. FOR SUPPORT IN THE SPECIFICATION, SEE APPLICANTS' MAY 23, 2000 AMENDMENT UNDER 37 C.F.R. §1.115, PAGE 187, LAST ¶ THROUGH PAGE 217, 1ST FULL ¶; SEE PARTICULARLY TABLE "SPECIFICATION REFERENCES TO NUCLEOTIDE ANALOGS" BEGINNING AT BOTTOM OF PAGE 188 AND CONTINUING THROUGH PAGE 191.</p> <p>Deletion of "self-indicating" in step (A)</p> <p>Insertion of "detectable" before "labeled fragments" in step (B)</p> <p>Insertion in providing step (B)(i), (B)(ii) and (B)(iii) of "or an analog of any of the foregoing," "a purine analog," "a 7-deazapurine analog," "or sugar analog," "or the pyrimidine analog," "or phosphate analog," "or base analog," which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA," "the sugar analog," "the phosphate analog," and "or the base analog thereof" N.B. FOR SUPPORT IN THE SPECIFICATION, SEE APPLICANTS' MAY 23, 2000 AMENDMENT UNDER 37 C.F.R. §1.115, PAGE 187, LAST ¶ THROUGH PAGE 217, 1ST FULL ¶; SEE PARTICULARLY TABLE "SPECIFICATION REFERENCES TO NUCLEOTIDE ANALOGS" BEGINNING AT BOTTOM OF PAGE 188 AND CONTINUING THROUGH PAGE 191.</p> <p>Insertion of "detectable" before "labeled fragments" in steps (C), (D) and (E).</p> |
| 1178 | | Same as Claim 570 above |
| 1179 | | Same as Claim 571 above |
| 1180 | | Same as Claim 572 above |
| 1181 | | Same as Claim 573 above |
| 1182 | | Same as Claim 574 above |
| 1183 | | Same as Claim 575 above |
| 1184 | | Same as Claim 576 above |
| 1185 | | Same as Claim 577 above |
| 1186 | | Same as Claim 578 above |
| 1187 | | Same as Claim 579 above |
| 1188 | | Same as Claim 580 above |
| 1189 | | Same as Claim 581 above |
| 1190 | | Same as Claim 582 above |
| 1191 | 359 | |
| 1192 | 360 | |
| 1193 | 361 | |
| 1194 | 362 | |
| 1195 | 346 | |
| 1196 | 347 | |
| 1197 | 365 | |
| 1198 | 366 | |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS |
|---------------------|---|--|
| | | (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
| 1199 | 359 & 366 | Claim 1199 combines Claim 359 ("incorporating step is carried out using an enzyme") and Claim 366 ("the labeled oligo- or polynucleotide of interest prepared by said incorporating step comprises at least one terminal modified nucleotide"). |
| 1200 | | Same as Claim 592 above |
| 1201 | | Same as Claim 593 above |
| 1202 | | Same as Claim 594 above |
| 1203 | | Same as Claim 595 above |
| 1204 | | Same as Claim 596 above |
| 1205 | | Same as Claim 597 above |
| 1206 | | Same as Claim 598 above |
| 1207 | | Same as Claim 599 above |
| 1208 | | Same as Claim 603 above |
| 1209 | | Same as Claim 604 above |
| 1210 | | Same as Claim 605 above |
| 1211 | | Same as Claim 606 above |
| 1212 | | Same as Claim 607 above |
| 1213 | | Same as Claim 608 above |
| 1214 | | New Claim 1214 recites the so-called "Ward" base labeling positions ("8-position of the purine moiety or the purine analog," "7-position of the deazapurine moiety or the 7-deazapurine analog," and "5-position of the pyrimidine moiety or the pyrimidine analog"). These positions are recited in other former and pending claims, including former claim 332 and pending New Claim 601, and others. Also, Ward's disclosure has also been incorporated by reference into the present application. See the Specification, Page 2, last ¶ ("The disclosures of this pending U.S. patent application Serial No. 255,223 are herein incorporated and made part of this application."). |
| 1215 | 559 | |
| 1216 | 560 | |
| 1217 | | See Claim 609 above |
| 1218 | 349 | |
| 1219 | 358 | |
| 1220 | 339 | |
| 1221 | 340 | |
| 1222 | 352 | |
| 1223 | 358 | Same as Claim 1219 above |
| 1224 | 339 | |
| 1225 | 340 | |
| 1226 | 355 | |
| 1227 | 358 | Same as Claims 1219 & 1223 above |
| 1228 | 339 | |
| 1229 | 340 | |
| 1230 | | Same as Claim 612 above |
| 1231 | | <i>ibid.</i> |
| 1232 | | Same as Claim 614 above |
| 1233 | | Same as Claim 615 above |
| 1234 | | Same as Claim 616 above |
| 1235 | | Same as Claim 617 above |
| 1236 | | Same as Claim 618 above |
| 1237 | | Same as Claim 619 above |
| 1238 | | Same as Claim 620 above |
| 1239 | 487 | |
| 1240 | 339 | |
| 1241 | 340 | |
| 1242 | 358 | Same as Claims 1219, 1223 & 1227 |
| 1243 | 412 | |
| 1244 | 531 | |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|----------------------------------|--|
| 1245 | 532 | |
| 1246 | 533 | |
| 1247 | 534 | |
| 1248 | 415 | |
| 1249 | 418 | |
| 1250 | 421 | |
| 1251 | 424 | |
| 1252 | 427 | |
| 1253 | 430 | |
| 1254 | 433 | |
| 1255 | 436 | |
| 1256 | 439 | |
| 1257 | 442 | |
| 1258 | 445 | |
| 1259 | 448 | |
| 1260 | 451 | |
| 1261 | 454 | |
| 1262 | 460 | |
| 1263 | 463 | |
| 1264 | | Same as Claim 657 above |
| 1265 | 385 & 539 | Same as Claim 658 above |
| 1266 | | Same as Claim 659 above |
| 1267 | 556 & 558 | New Claim 1267 recites "wherein said heterocyclic aromatic compound is fluorescent." Former claims 556 & 558 recited "wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent." |
| 1268 | 469 | |
| 1269 | | Same as Claim 1268 above. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 1268. |
| 1270 | 418 | |
| 1271 | 303 | |
| 1272 | 469 | Same as Claim 1268 above |
| 1273 | | Same as Claim 1272 above. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 1272. |
| 1274 | 472 | |
| 1275 | 475 | |
| 1276 | 478 | |
| 1277 | 481 | |
| 1278 | 334 | But note that the base sequencing claims for former claim 334 were different from the base sequencing claim for New Claim 1278. |
| 1279 | 487 | |
| 1280 | 490 | |
| 1281 | 497 | |
| 1282 | 500 | |
| 1283 | 503 | |
| 1284 | 506 | |
| 1285 | 368 | |
| 1286 | 369 | |
| 1287 | 370 | But note that the term "one or more self-indicating molecules" in former claim 370 has been changed to "one or more indicator molecules" in New Claim 1287. |
| 1288 | 371 | |
| 1289 | 372 | But note that addition of the term "or nucleotide analogs" in New Claim 1289. |
| 1290 | 369 | |
| 1291 | 418 | But see Claim 714 above for support of "a chromogenic compound." |
| 1292 | 448 | Note that the term "enzyme" is recited as a Markush member in New Claim 1291 from which New Claim 1292 depends. |

| NEW CLAIM NO. | FORMER CLAIM NO. IF APPLICABLE | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|--------------------------------|--|
| 1293 | | Same as Claim 716 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 716 IS DIFFERENT FROM NEW CLAIM 1293. |
| 1294 | 416-417 | Same as Claim 717 above BUT NOTE THAT THE BASE SEQUENCING CLAIM FOR NEW CLAIM 717 IS DIFFERENT FROM NEW CLAIM 1294. |
| 1295 | | TO BE ADDRESSED IN A FUTURE RESPONSE |
| 1296 | | Specification, Page 88, 2nd ¶; See in particular 2nd sentence ("By way of example, one can fix to a solid matrix a specific antigen and bind to this antigen an antibody directed against this antigen which itself has been biotinylated.") |
| 1297 | 334 & 416-417 | Same as Claim 719 above. NOTE THAT THE BASE CLAIM FOR NEW CLAIM 719 IS A SEQUENCING PROCESS WHICH IS DIFFERENT FROM THE BASE CLAIM FOR NEW CLAIM 1297 WHICH IS A DETECTION PROCESS. |
| 1298 | 284 | Insertion in Step (a) of "specifically" before "hybridizing" in New Claim 1298. Insertion in Step (a) of "detectable" before "oligo- or polynucleotides" in New Claim 1298 Insertion in Step (a) of "or nucleotide analogs," "which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA," "the sugar analog," "the phosphate analog," and "or the base analog thereof" N.B. FOR SUPPORT IN THE SPECIFICATION, SEE APPLICANTS' MAY 23, 2000 AMENDMENT UNDER 37 C.F.R. §1.115, PAGE 187, LAST ¶ THROUGH PAGE 217, 1ST FULL ¶; SEE PARTICULARLY TABLE "SPECIFICATION REFERENCES TO NUCLEOTIDE ANALOGS" BEGINNING AT BOTTOM OF PAGE 188 AND CONTINUING THROUGH PAGE 191. Insertion of "non-radioactively" after "detecting" Step (b). |
| 1299 | | Specification, Page 3, 2nd ¶, Page 8, last three lines, through Page 9, 1st two lines & Page 14, penultimate ¶ ("... when ... incorporated into a double-stranded ribonucleic acid, deoxyribonucleic acid duplex, or DNA-RNA hybrid;") Specification, Page 98, 2nd ¶ ("... Such probes would contain a nucleotide sequence substantially matching the DNA or RNA sequence of genetic material to be located and/or identified. . . A probe having a desired nucleotide sequence, such as a single-stranded polynucleotide, either DNA or RNA probe, would then be brought into contact with DNA or RNA genetic material to be identified.") Specification, Page 99, first two lines ("... to effect an identification of most of the DNA or RNA material to be investigated or identified, . . SEE ALSO ORIGINALLY FILED CLAIMS 51-54 AND 190 ("DOUBLE-STRANDED DNA, RNA OR DNA-RNA HYBRID.")) |
| 1300 | | See originally filed claims 48-50 ("single-stranded polynucleotide") and 51-54 ("double-stranded polynucleotide"). |
| 1301 | | Specification, Page 98, 2nd ¶; see in particular the 3rd sentence in the paragraph ("A probe having a desired nucleotide sequence, such as a single-stranded polynucleotide, either DNA or RNA probe, would then be brought into contact with DNA or RNA genetic material to be identified. Upon localization of the probe and the formation of a double-stranded polynucleotide and the matching DNA or RNA material to be identified, the resulting formed double-stranded DNA or RNA-containing material would then be observable and identified.") |
| 1302 | 318 | Same as Claim 570 above |
| 1303 | 319 | Same as Claim 575 above |
| 1304 | | Same as Claim 571 above |
| 1305 | 318 | Same as Claim 574 above |
| 1306 | 320 | |
| 1307 | 321 | |
| 1308 | 513 | |
| 1309 | 518 | |
| 1310 | 322 | |
| 1311 | 323 | |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|----------------------------------|--|
| 1312 | 519 | |
| 1313 | 324 | |
| 1314 | 325 | |
| 1315 | 326 | |
| 1316 | 327 | |
| 1317 | 328 | |
| 1318 | | Same as Claim 591 above BUT NOTE THAT NEW CLAIM 591 IS DIRECTED TO A SEQUENCING PROCESS CLAIM AND NEW CLAIM 1318 IS DIRECTED TO A DETECTION PROCESS CLAIM. |
| 1319 | | Same as Claim 592 above |
| 1320 | | Same as Claim 593 above |
| 1321 | | Same as Claim 594 above |
| 1322 | | Same as Claim 595 above |
| 1323 | | Same as Claim 596 above |
| 1324 | | Same as Claim 597 above |
| 1325 | | Same as Claim 598 above |
| 1326 | | <i>ibid.</i> |
| 1327 | | Same as Claim 603 above |
| 1328 | | Same as Claim 604 above |
| 1329 | | Same as Claim 605 above |
| 1330 | | Same as Claim 606 above |
| 1331 | | Same as Claim 607 above |
| 1332 | | Same as Claim 608 above |
| 1333 | | See Claim 609 above |
| 1334 | 535 | |
| 1335 | 536 | |
| 1336 | | Same as Claim 612 above |
| 1337 | | <i>ibid.</i> |
| 1338 | | Same as Claim 614 above |
| 1339 | | Same as Claim 615 above |
| 1340 | | Same as Claim 616 above |
| 1341 | | Same as Claim 617 above |
| 1342 | | Same as Claim 618 above |
| 1343 | | Same as Claim 619 above |
| 1344 | | Same as Claim 620 above |
| 1345 | 308 | |
| 1346 | 339 | |
| 1347 | 340 | |
| 1348 | | See originally filed claim 104 ("wherein said Sig chemical moiety is attached to the S sugar moiety such that an oligoribonucleotide or polyribonucleotide containing such ribonucleotide is capable of forming a double-stranded ribonucleic acid or a DNA-RNA hybrid . . .") |
| 1349 | 309 | |
| 1350 | 285 | |
| 1351 | 531 | |
| 1352 | 532 | |
| 1353 | 533 | |
| 1354 | 540 | Note that former claim 540 depends from a sequencing process (claim 329) and New Claim 1354 depends from a detection process |
| 1355 | 534 | |
| 1356 | 542 | Note that former claim 542 depends from a sequencing process (claim 329) and New Claim 1356 depends from a detection process |
| 1357 | 286 | |
| 1358 | 287 | |
| 1359 | 288 | |
| 1360 | 289 | |
| 1361 | 290 | |
| 1362 | 291 | |

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| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|----------------------------------|--|
| 1363 | 292 | |
| 1364 | 293 | |
| 1365 | 294 | |
| 1366 | 295 | |
| 1367 | 296 | |
| 1368 | 297 | |
| 1369 | 298 | |
| 1370 | 299 | |
| 1371 | 301 | |
| 1372 | 302 | |
| 1373 | 385 | Note that former claim 385 was directed to a chromosomal characterization process, whereas New Claim 1373 is directed to a detection process. The term "indicator molecule" was also recited in several former dependent claims. See, e.g., former claims 386, 391-392, 401-402 and 404-406. |
| 1374 | 385 & 539 | Same as Claim 658 above |
| 1375 | | Same as Claim 659 above |
| 1376 | 556 & 558 | Same as Claim 1267 above. BUT NOTE THAT THE BASE CLAIM FOR CLAIM 1267 IS A SEQUENCING PROCESS WHEREAS THE BASE CLAIM FOR CLAIM 1376 IS A DETECTION PROCESS. |
| 1377 | 304 | |
| 1378 | | Same as Claim 1377 above. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 1377. |
| 1379 | 303 | |
| 1380 | 304 | Same as Claim 1377 above |
| 1381 | 304 | Same as Claim 1380 above. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 1380. |
| 1382 | 305 | |
| 1383 | 306 | |
| 1384 | 287 | That "Sig comprises an antibody component" as recited in New Claim 1384 was also recited in former dependent claim 287, together with other Markush members. |
| 1385 | 287 | That "Sig comprises a chelating component" as recited in New Claim 1385 was also recited as a Markush member in former claim 287. |
| 1386 | 333 | But note the change from "self-indicating modified nucleotide" in former claim 333 to "indicator molecule" in New Claim 1386. |
| 1387 | 317 | The term "chelating component" recited in New Claim 1387 is also recited as a Markush member in former claim 317 as well as New Claim 1358. |
| 1388 | 307 | |
| 1389 | 308 | |
| 1390 | 309 | |
| 1391 | 310 | Except for deletion of Sig from structural formula |
| 1392 | 311 | Except for deletion of Sig from structural formula |
| 1393 | 312 | |
| 1394 | 313 | |
| 1395 | 314 | |
| 1396 | 315 | |
| 1397 | 316 | |
| 1398 | 317 | |
| 1399 | | Same as Claim 709 above |
| 1400 | 385 | Same as Claim 657 above |
| 1401 | 371 | BUT NOTE THAT FORMER CLAIM 371 WAS DIRECTED TO A SEQUENCING PROCESS CLAIM AND NEW CLAIM 1401 IS DIRECTED TO A DETECTION PROCESS. |
| 1402 | 372 | BUT NOTE THAT FORMER CLAIM 372 WAS DIRECTED TO A SEQUENCING PROCESS CLAIM AND NEW CLAIM 1402 IS DIRECTED TO A DETECTION PROCESS. |
| 1403 | 369 | |
| 1404 | 287 | But see Claim 714 above for support of "a chromogenic compound." |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|----------------------------------|--|
| 1405 | 448 | Note that the term "enzyme" is recited as a Markush member in New Claim 1398. ALSO NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 448 WAS A SEQUENCING DETECTION CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1405 IS A DETECTION PROCESS CLAIM. |
| 1406 | | <p><u>Support for Indirect Detection</u></p> <p>Page 6, Penultimate ¶ ("These various utilities are based upon the ability of the molecules to form stable complexes with polypeptides which in turn can be detected, either by means of properties inherent in the polypeptide or by means of detectable moieties which are attached to, or which interact with, the polypeptide.")</p> <p>Page 7, last three lines, through Page 8, 1st two lines ("... It is preferable that the probe moiety be attached ... so that it can readily interact with antibodies, other detector proteins, or chemical reagents.")</p> <p>Page 25, penultimate ¶, through Page 26, 1st ¶ ("The various modified nucleotides, oligonucleotides, and polynucleotides of this invention may be detected by contacting the compounds with polypeptides ... [which] include one or more moieties which can be detected ... One polypeptide detector for the blotting-type probe is avidin. ... If avidin is coupled to potentially demonstrable indicator molecules, ...")</p> <p>Page 26, last ¶, through Page 27, 1st ¶ ("A most preferred protein for biotin-like probe detection is monospecific rabbit IgG, anti-biotin immunoglobulin. ... anti-biotin antibodies have proven extremely useful in detecting specific polynucleotide sequences on chromosomes ...")</p> <p>Page 30, 1st & 2nd ¶ ("... Hybridized nucleic acid duplexes are then identified by forming a complex between the duplex and a suitable polypeptide which carries a detectable moiety. ... can be detected following hybridization with a polynucleotide probe according to this invention based upon complex formation with a suitable detectable polypeptide.")</p> <p>Page 31, last line, through Page 32, 1st line ("... as detected by indirect immunofluorescence for <u>in situ</u> mapping.")</p> <p>Page 33, 1st full ¶ ("Indirect immunofluorescence")</p> <p>Page 36, last ¶ ("An alternative to the fluorescence method for visualizing hybridized probes is to direct enzymes such as peroxidase, alkaline phosphatase or (sic) β-galactosidase to the hybridization site where enzymatic conversion of soluble substrates to insoluble colored precipitates permits light microscope visualization.")</p> <p>Page 38, 1st ¶ ("These polynucleotides are hybridized ... and the resulting duplexes contacted with appropriate polypeptides ... [which] include detectable moieties ...")</p> |
| 1407 | 287 | New Claim 1407 recites selected Markush members from former claim 287. NOTE THAT "LIGAND" RECITED IN NEW CLAIM 1407 IS ALSO FOUND IN FORMER DEPENDENT CLAIMS 504-506, THE LATTER CLAIMS BEING DRAWN TO SEQUENCING PROCESSES. |
| 1408 | | TO BE ADDRESSED IN A FUTURE RESPONSE |
| 1409 | | Same as Claim 1297 above BUT TO BE ADDRESSED IN PART IN A FUTURE RESPONSE |
| 1410 | 510 | See also Specification, Page 32, 1st full ¶ ("After the final 2 X SSC wash to remove unhybridized probe, ...") |
| 1411 | 396 | Specification, Page 77, Example XXXIV ("A DNA probe was ligated to a synthetic DNA composed of repeated sequences of <i>E. coli</i> lac operator DNA. After hybridization to detect antiprobe sequences, the hybridized DNA was detected by reaction with biotinylated lac repressor which was, in turn, detected by an enzyme linked Immuno sorbent assay using goat anti-biotin IGG to react with the biotin and a second antibody coupled to horse radish peroxidase. ...") |
| 1412 | | Same as Claim 1299 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1299 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1412. |

| NEW CLAIM NO. | FORMER CLAIM NO. IF APPLICABLE | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
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| 1413 | | Same as Claim 1300 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1300 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1413. |
| 1414 | | Same as Claim 1301 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1301 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1414. |
| 1415 | | Same as Claim 1302 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1302 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1415. |
| 1416 | | Same as Claim 1303 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1303 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1416. |
| 1417 | | Same as Claim 1304 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1304 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1417. |
| 1418 | | Same as Claim 1305 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1305 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1418. |
| 1419 | | Same as Claim 1306 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1306 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1419. |
| 1420 | | Same as Claim 1307 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1307 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1420. |
| 1421 | | Same as Claim 1308 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1308 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1421. |
| 1422 | | Same as Claim 1309 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1309 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1422. |
| 1423 | | Same as Claim 1310 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1310 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1423. |
| 1424 | | Same as Claim 1311 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1311 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1424. |
| 1425 | | Same as Claim 1312 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1312 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1425. |
| 1426 | | Same as Claim 1313 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1313 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1426. |
| 1427 | | Same as Claim 1314 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1314 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1427. |
| 1428 | | Same as Claim 1315 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1315 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1428. |
| 1429 | | Same as Claim 1317 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1317 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1429. |
| 1430 | 399 | |
| 1431 | 400 | See also the Specification, Pages 77-78, Example XXXIV ("A DNA probe was ligated to a synthetic DNA composed of repeated sequences of <i>E. coli</i> lac operator DNA. . . The lac operator DNA has been described by Caruthers (Second Annual Congress for Recombinant DNA Research, Los Angeles, 1982), and it was ligated, in a blunt end ligation, using T4 ligase, to a adenovirus DNA probe.") |
| 1432 | 397 | |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS |
|---------------|----------------------------------|---|
| | | (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
| 1433 | 398 | See also the Specification, Pages 77-78, Example XXXIV ("A DNA probe was ligated to a synthetic DNA . . . The lac operator DNA has been described by Caruthers (Second Annual Congress for Recombinant DNA Research, Los Angeles, 1982), and it was ligated, in a blunt end ligation, using T4 ligase, to a adenovirus DNA probe.") |
| 1434 | | See Claim 612 above ("such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.") |
| 1435 | | See Claim 616 above ("said covalent attachment . . . does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal.") |
| 1436 | | Same as Claim 1341 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1341 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1436. |
| 1437 | | Same as Claim 1342 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1342 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1437. |
| 1438 | | Same as Claim 1343 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1343 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1438. |
| 1439 | | Same as Claim 1344 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1344 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1439. |
| 1440 | 397 | See also Claim 1345 above (" . . . covalently attached . . . through a linkage group.") BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1345 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1440. |
| 1441 | | <i>ibid.</i> |
| 1442 | 339 | |
| 1443 | 340 | |
| 1444 | | See Claim 1434 above |
| 1445 | 370 | Same as Claim 1400 BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1400 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1445. ALSO NOTE THE TERM "SIGNALING COMPONENT" HAS BEEN INSERTED IN NEW CLAIM 1445. |
| 1446 | 285 | BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR FORMER CLAIM 285 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1446. |
| 1447 | 531 | |
| 1448 | 532 | |
| 1449 | 533 | |
| 1450 | 540 | Note that former claim 540 depends from a sequencing process (claim 329) and 1450 depends from a detection process |
| 1451 | 534 | |
| 1452 | 542 | Note that former claim 542 depends from a sequencing process (claim 329) and 1452 depends from a detection process |
| 1453 | 286 | BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR FORMER CLAIM 286 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1453. |
| 1454 | 287 | See also Claim 1398 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIMS FOR FORMER CLAIM 287 AND NEW CLAIM 1398 ARE DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1454. |
| 1455 | 533 & 534 | Former Claims 533 & 534 both recited "said Sig detectable moiety comprises an aromatic . . . group comprising at least . . . carbon atoms.") |
| 1456 | | Same as Claim 659 above |
| 1457 | 556 & 558 | Same as Claim 1376 above. BUT NOTE THAT THE BASE CLAIMS FOR CLAIMS 1376 AND 1457 ARE FOR DIFFERENT DETECTION PROCESSES. |
| 1458 | 304 | But note that the base detection claims for claims 304 and 1458 are different. |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
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| 1459 | | Same as Claim 1458 above. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 1458. |
| 1460 | 305 | Former claim 305 recited "Sig comprises a chemiluminescent component." BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR FORMER CLAIM 305 WAS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1460. |
| 1461 | 287 | Former claim 287 recited "a chelating component" in the Markush members for Sig. BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR FORMER CLAIM 287 WAS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1461. |
| 1462 | 334 | But note that the base claim for former claim 334 was a sequencing detection process and the base claim for New Claim 1462 is a detection process claim. |
| 1463 | | See Claim 1388 above BUT NOTE THAT THE BASE DETECTION CLAIM FOR NEW CLAIM 1388 IS DIFFERENT FROM THE BASE DETECTION CLAIM FOR NEW CLAIM 1463. |
| 1464 | | See Claim 1389 above BUT NOTE THAT THE BASE DETECTION CLAIM FOR NEW CLAIM 1389 IS DIFFERENT FROM THE BASE DETECTION CLAIM FOR NEW CLAIM 1464. |
| 1465 | | Specification, Pages 77-78, Example XXXIV ("A DNA probe was ligated to a synthetic DNA composed of repeated sequences of <i>E. coli</i> lac operator DNA. After hybridization to detect antiprobe sequences, the hybridized DNA was detected by reaction with biotinylated lac repressor which was, in turn, detected by an enzyme linked immuno sorbent assay using goat anti biotin IGG to react with the biotin and a second antibody coupled to horse radish peroxidase. . .") |
| 1466 | | Same as Claim 709 above |
| 1467 | | Same as Claim 1400 above BUT NOTE THAT THE BASE DETECTION CLAIM FOR NEW CLAIM 1400 IS DIFFERENT FROM THE BASE DETECTION CLAIM FOR NEW CLAIM 1469. ALSO NOTE THAT THE TERM "SIGNALING COMPONENTS" HAS BEEN INSERTED INTO NEW CLAIM 1469. |
| 1468 | 287 | Same as Claim 1404 above BUT NOTE THAT THE BASE DETECTION CLAIM FOR NEW CLAIM 1468 IS DIFFERENT FROM THE BASE DETECTION CLAIM FOR NEW CLAIM 1404. |
| 1469 | | Same as Claim 1406 above BUT NOTE THAT THE BASE DETECTION CLAIM FOR NEW CLAIM 1406 IS DIFFERENT FROM THE BASE DETECTION CLAIM FOR NEW CLAIM 1469. |
| 1470 | | TO BE ADDRESSED IN A FUTURE RESPONSE |
| 1471 | | Same as Claim 1297 above |
| 1472 | | Same as Claim 1410 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1410 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1472. |
| 1473 | 376 | Insertion of "detectable" before "modified or labeled nucleotides . . ." Insertion of "or nucleotide analogs," "which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA," "or sugar analog," "or phosphate analog," and "or an analog of any of the foregoing thereof" [after "BASE"]. N.B. FOR SUPPORT IN THE SPECIFICATION, SEE APPLICANTS' MAY 23, 2000 AMENDMENT UNDER 37 C.F.R. § 1.115, PAGE 187, LAST ¶ THROUGH PAGE 217, 1ST FULL ¶; SEE PARTICULARLY TABLE "SPECIFICATION REFERENCES TO NUCLEOTIDE ANALOGS" BEGINNING AT BOTTOM OF PAGE 188 AND CONTINUING THROUGH PAGE 191. Insertion of "non-radioactively" after last "detecting" step |

| NEW CLAIM NO. | FORMER CLAIM NO. IF APPLICABLE | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|--------------------------------|--|
| 1474 | 381 | Insertion of "detectable" before "modified or labeled nucleotides . . ." Insertion of "or nucleotide analogs," "which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA," "or sugar analog," "or phosphate analog," and "or an analog of any of the foregoing thereof" [after "BASE"]. N.B. FOR SUPPORT IN THE SPECIFICATION, SEE APPLICANTS' MAY 23, 2000 AMENDMENT UNDER 37 C.F.R. § 1.115, PAGE 187, LAST ¶ THROUGH PAGE 217, 1ST FULL ¶; SEE PARTICULARLY TABLE "SPECIFICATION REFERENCES TO NUCLEOTIDE ANALOGS" BEGINNING AT BOTTOM OF PAGE 188 AND CONTINUING THROUGH PAGE 191. Insertion of "non-radioactively" after last "detecting" step |
| 1475 | 385 | Insertion of "detectable" before "modified or labeled nucleotides . . ." Insertion of "or nucleotide analogs," "which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA," "or sugar analog," "or phosphate analog," and "or an analog of any of the foregoing thereof" [after "BASE"]. N.B. FOR SUPPORT IN THE SPECIFICATION, SEE APPLICANTS' MAY 23, 2000 AMENDMENT UNDER 37 C.F.R. § 1.115, PAGE 187, LAST ¶ THROUGH PAGE 217, 1ST FULL ¶; SEE PARTICULARLY TABLE "SPECIFICATION REFERENCES TO NUCLEOTIDE ANALOGS" BEGINNING AT BOTTOM OF PAGE 188 AND CONTINUING THROUGH PAGE 191. Insertion of "non-radioactively" after last "detecting" step |
| 1476 | 390 | Insertion of "detectable" before "modified or labeled nucleotides . . ." Insertion of "or nucleotide analogs," "which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA," "or sugar analog," "or phosphate analog," and "or an analog of any of the foregoing thereof" [after "BASE"]. N.B. FOR SUPPORT IN THE SPECIFICATION, SEE APPLICANTS' MAY 23, 2000 AMENDMENT UNDER 37 C.F.R. § 1.115, PAGE 187, LAST ¶ THROUGH PAGE 217, 1ST FULL ¶; SEE PARTICULARLY TABLE "SPECIFICATION REFERENCES TO NUCLEOTIDE ANALOGS" BEGINNING AT BOTTOM OF PAGE 188 AND CONTINUING THROUGH PAGE 191. Insertion of "non-radioactively" after last "detecting" step |
| 1477 | | Same as Claim 1318 above BUT NOTE THAT THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1318 IS DIFFERENT FROM THE BASE DETECTION PROCESS CLAIM FOR NEW CLAIM 1477. |
| 1478 | | Same as Claim 592 above |
| 1479 | | Same as Claim 593 above |
| 1480 | | Same as Claim 594 above |
| 1481 | | Same as Claim 595 above |
| 1482 | | Same as Claim 596 above |
| 1483 | | Same as Claim 597 above |
| 1484 | | Same as Claim 598 above |
| 1485 | | <i>Ibid.</i> |
| 1486 | | Same as Claim 603 above |
| 1487 | | Same as Claim 604 above |
| 1488 | | Same as Claim 605 above |
| 1489 | | Same as Claim 606 above |
| 1490 | | Same as Claim 607 above |
| 1491 | | Same as Claim 608 above |
| 1492 | | Same as Claim 609 above |
| 1493 | 535 | |
| 1494 | 536 | |
| 1495 | | Same as Claim 612 above |
| 1496 | | <i>Ibid.</i> |
| 1497 | | Same as Claim 614 above |
| 1498 | | Same as Claim 615 above |
| 1499 | | Same as Claim 616 above |
| 1500 | | Same as Claim 617 above |
| 1501 | | Same as Claim 618 above |
| 1502 | | Same as Claim 619 above |
| 1503 | | Same as Claim 620 above |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|----------------------------------|---|
| 1504 | 308 | Same as Claim 1345 above |
| 1505 | 339 | |
| 1506 | 340 | |
| 1507 | 309 | Same as Claim 1349 above. But note that Claim 1507 is directed to chromosomal characterization processes and Claim 1349 is directed to a detection process. |
| 1508 | 285 | Note that New Claim 1508 is directed to chromosomal characterization processes, whereas former claim 285 depended from a detection process. |
| 1509 | 531 | |
| 1510 | 532 | |
| 1511 | 533 | |
| 1512 | 540 | Note that former claim 540 depended from a sequencing process (claim 329) and New Claim 1452 depends from a chromosomal characterization process |
| 1513 | 534 | |
| 1514 | 542 | Note that former claim 542 depended from a sequencing process (claim 329) and New Claim 1452 depends from a chromosomal characterization process |
| 1515 | 286 | Note that former claim 286 was directed to a detection process, whereas New Claim 1515 is directed to chromosomal characterization processes. |
| 1516 | 287 | Note that former claim 287 was directed to a detection process, whereas New Claim 1516 is directed to chromosomal characterization processes. |
| 1517 | 288 | Note that former claim 288 was directed to a detection process, whereas New Claim 1517 is directed to chromosomal characterization processes. |
| 1518 | 289 | Note that former claim 289 was directed to a detection process, whereas New Claim 1518 is directed to chromosomal characterization processes. |
| 1519 | 290 | Note that former claim 290 was directed to a detection process, whereas New Claim 1519 is directed to chromosomal characterization processes. |
| 1520 | 291 | Note that former claim 291 was directed to a detection process, whereas New Claim 1520 is directed to chromosomal characterization processes. |
| 1521 | 292 | Note that former claim 292 was directed to a detection process, whereas New Claim 1521 is directed to chromosomal characterization processes. |
| 1522 | 293 | Same as Claim 1364 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1364 AND FORMER CLAIM 293 WERE FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1522 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1523 | 294 | Same as Claim 1365 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1365 AND FORMER CLAIM 294 WERE FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1523 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1524 | 295 | Same as Claim 1366 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1366 AND FORMER CLAIM 295 WERE FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1524 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1525 | 296 | Same as Claim 1367 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1367 AND FORMER CLAIM 296 WERE FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1525 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |

| NEW CLAIM NO. | FORMER CLAIM NO. IF APPLICABLE | <u>COMMENTS</u> (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|--------------------------------|---|
| 1526 | 297 | Same as Claim 1368 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1368 AND FORMER CLAIM 297 WERE FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1526 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1527 | 298 | Same as Claim 1369 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1369 AND FORMER CLAIM 298 WERE FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1527 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1528 | 299 | Same as Claim 1370 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1370 AND FORMER CLAIM 299 WERE FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1528 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1529 | 301 | Same as Claim 1371 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1371 AND FORMER CLAIM 301 WERE FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1529 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1530 | 302 | Same as Claim 1372 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1372 AND FORMER CLAIM 296 WERE FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1530 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1531 | 385 | Note that the term "indicator molecule" was also recited in several former dependent claims. See, e.g., former claims 386, 391-392, 401-402 and 404-406. |
| 1532 | | Same as Claim 658 above |
| 1533 | | Same as Claim 659 above |
| 1534 | 556 & 558 | Same as Claim 1376 above. BUT NOTE THAT THE BASE CLAIM FOR CLAIM 1376 IS FOR A DETECTION PROCESS, WHEREAS THE BASE CLAIM FOR CLAIM 1534 IS FOR A CHROMOSOMAL CHARACTERIZATION PROCESS. |
| 1535 | 304 | But note that the base claim for claim 304 is a detection process and the base claim for claim 1535 is for chromosomal characterization processes. |
| 1536 | | Same as Claim 1535 above. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 1535. |
| 1537 | | Same as Claim 1379 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1379 IS A DETECTION PROCESS AND THAT THE BASE CLAIMS FOR NEW CLAIM 1537 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1538 | 304 | Same as Claim 1535 above |
| 1539 | | Same as Claim 1538 above. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 1538. |
| 1540 | 305 | Same as Claim 1340 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1340 IS A DETECTION PROCESS AND THAT THE BASE CLAIMS FOR NEW CLAIM 1540 ARE CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1541 | 306 | Same as Claim 1383 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1383 IS A DETECTION PROCESS AND THAT THE BASE CLAIMS FOR NEW CLAIM 1541 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1542 | 287 | Same as Claim 1384 above. That "Sig comprises an antibody component" as recited in New Claim 1542 was also recited in former dependent claim 287, together with other Markush members. BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1384 IS A DETECTION PROCESS AND THAT THE BASE CLAIMS FOR NEW CLAIM 1542 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1543 | 287 | Same as Claim 1385 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1385 IS A DETECTION PROCESS AND THAT THE BASE CLAIMS FOR NEW CLAIM 1543 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|----------------------------------|--|
| 1544 | 386 & 391-392 | Indicator molecules are recited in former claims 386 & 391 ("each of said sets of clones or DNA fragments or oligo- or polynucleotides is labeled with the same indicator molecule."), former claim 392 ("each of said sets of clones or DNA fragments or oligo- or polynucleotides is labeled with a different indicator molecule."), and former claim 402 ("wherein said providing step each oligo- or polynucleotide is labeled with the same or a different indicator molecule.") See also Claim 657 above. |
| 1545 | 333 | Same as Claim 1386 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1386 IS A DETECTION PROCESS AND THAT THE BASE CLAIMS FOR NEW CLAIM 1545 ARE CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1546 | 334 | Same as Claim 1387 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1387 IS FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1546 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1547 | 307 | Same as Claim 1388 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1388 IS FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1547 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1548 | 308 | Same as Claim 1389 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1389 IS FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1548 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1549 | 309 | Same as Claim 1390 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1390 IS FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1549 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1550 | | Same as Claim 1391 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1391 IS FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1550 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1551 | | Same as Claim 1392 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1392 IS FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1551 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1552 | 312 | Same as Claim 1393 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1393 IS FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1552 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1553 | 313 | Same as Claim 1394 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1394 IS FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1553 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1554 | 314 | Same as Claim 1395 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1395 IS FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1554 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1555 | 314 | Same as Claim 1395 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1395 IS FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1555 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1556 | 315 | Same as Claim 1396 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1396 IS FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1556 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1557 | 315 | Same as Claim 1396 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1396 IS FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1557 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1558 | 316 | Same as Claim 1397 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1397 IS FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1558 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1559 | 317 | Same as Claim 1398 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1398 IS FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1559 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1560 | | Same as Claim 1399 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1399 IS FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1560 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|----------------------------------|---|
| 1561 | | Same as Claim 1400 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1400 IS FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1561 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. NOTE THAT NEW CLAIM 1561 RECITES "WHEREIN SAID DIRECT DETECTION IS CARRIED OUT ON ONE OR MORE INDICATOR MOLECULES" AND NEW CLAIM 1400 RECITES "WHEREIN SAID DIRECT DETECTION IS CARRIED OUT ON ONE OR MORE NUCLEOTIDES OR NUCLEOTIDE ANALOGS COMPRISING INDICATOR MOLECULES.") |
| 1562 | | Same as Claim 1401 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1401 IS FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1562 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1563 | | Same as Claim 1402 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1402 IS FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1563 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1564 | | Same as Claim 1403 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1403 IS FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1564 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1565 | 511-512 | |
| 1566 | | Same as Claim 1405 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1405 IS FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1566 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1567 | | Same as Claim 1406 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1406 IS FOR A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1567 ARE FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1568 | | New Claim 1568 recites selected Markush members from former claims 511-512. NOTE THAT "LIGAND" RECITED IN NEW CLAIM 1568 IS ALSO FOUND IN FORMER DEPENDENT CLAIMS 504-506, THE LATTER CLAIMS BEING DRAWN TO SEQUENCING PROCESSES. |
| 1569 | | TO BE ADDRESSED IN A FUTURE RESPONSE |
| 1570 | | Same as Claim 1297 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1297 IS A DETECTION PROCESS AND THAT THE BASE CLAIMS FOR NEW CLAIM 1570 ARE CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1571 | | Same as Claims 1410 and 1472 above. NOTE THAT THE BASE CLAIMS FOR NEW CLAIMS 1410 AND 1472 ARE DETECTION PROCESSES AND THAT THE BASE CLAIMS FOR NEW CLAIM 1571 IS FOR CHROMOSOMAL CHARACTERIZATION PROCESSES. |
| 1572 | 377 | |
| 1573 | 386 | |
| 1574 | 378, 382 & 387 | |
| 1575 | 379, 383 & 388 | |
| 1576 | 380, 384 & 389 | |
| 1577 | 402 | With Claim 1577 limited to the "same indicator molecule" |
| 1578 | 402 | With Claim 1578 limited to a "different indicator molecule" |
| 1579 | 393 | |
| 1580 | 394 | |
| 1581 | 395 | |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|----------------------------------|---|
| 1582 | 337 | <p>Insertion of "detectable non-radioactively" before "labeled oligo- or polynucleotide" in the preamble</p> <p>Insertion of "detectable" and "or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA" in providing step (A)(1)</p> <p>Substitution of "wherein said chemically modified or labeled nucleotides or nucleotide analogs comprise one or more signaling moieties which are capable of providing directly or indirectly a detectable non-radioactive signal" for "chemical modification" in element (1) of providing step (A).</p> <p>Insertion of "detectable" before "chemically modified" in providing step (A)(2)</p> <p>Insertion of "or nucleotide analogs," "the sugar analog," "the phosphate moiety," "or the base analog" preceding component (i)</p> <p>Insertion of "or phosphate analog," "or sugar analog," "or a base analog of any of the foregoing," "or an analog thereof," "detectable" [before non-radioactive moiety in definition of "Sig"] in components (i), (ii) and (iii)</p> |
| 1583 | | Same as Claim 570 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 571 IS A SEQUENCING DETECTION CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1583 IS FOR A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1584 | | Same as Claim 574 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 571 IS A SEQUENCING DETECTION CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1583 IS FOR A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1585 | | Same as Claim 575 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 571 IS A SEQUENCING DETECTION CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1583 IS FOR A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1586 | | Same as Claim 576 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 571 IS A SEQUENCING DETECTION CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1583 IS FOR A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1587 | | Same as Claim 577 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 571 IS A SEQUENCING DETECTION CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1583 IS FOR A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1588 | | Same as Claim 578 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 571 IS A SEQUENCING DETECTION CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1583 IS FOR A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1589 | | Same as Claim 579 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 571 IS A SEQUENCING DETECTION CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1583 IS FOR A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1590 | | Same as Claim 580 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 571 IS A SEQUENCING DETECTION CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1583 IS FOR A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1591 | | Same as Claim 581 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 571 IS A SEQUENCING DETECTION CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1583 IS FOR A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1592 | | Same as Claim 582 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 571 IS A SEQUENCING DETECTION CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1583 IS FOR A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |

| NEW CLAIM NO. | FORMER CLAIM NO. IF APPLICABLE | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|--------------------------------|--|
| 1593 | | Same as Claim 571 above EXCEPT FOR ADDITION OF TERM "LIVING." ALSO NOTE THAT THE BASE CLAIM FOR NEW CLAIM 571 IS A SEQUENCING DETECTION CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1583 IS FOR A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1594 | | Same as Claim 572 above EXCEPT FOR ADDITION OF TERM "LIVING." ALSO NOTE THAT THE BASE CLAIM FOR NEW CLAIM 571 IS A SEQUENCING DETECTION CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1583 IS FOR A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1595 | | Same as Claim 573 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 571 IS A SEQUENCING DETECTION CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1583 IS FOR A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1596 | 342 | |
| 1597 | 343 | |
| 1598 | 344 | |
| 1599 | | Specification, Page 20, 1st ¶ ("... biotin-labeled RNA probes can be prepared enzymatically using RNA ligase with compounds such as biotinyl-pCp.") Specification, Page 25, 1st two ¶s ("These compounds can be made by enzymatic polymerization of appropriate nucleotides, especially nucleotide triphosphates ... Also, the compounds can be prepared by terminal addition to oligo- or polynucleotides to produce compounds in which m or n is 0 depending upon whether the addition is at the 5' or 3' position.") Specification, Page 99, last ¶, through Page 100, last ¶ ("One particularly useful technique ... involves the utilization of terminal transferase for the addition of biotinylated dUMP onto the 3' ends of a polypyrimidine or to single-stranded DNA.) SEE ALSO SPECIFICATION, PAGE 99, LAST ¶, LINES 6-8 FROM THE BOTTOM OF THE PAGE. SEE ALSO PAGE, 100, 2ND ¶ ("... BIOTINATED dUTP WAS ADDED TO THE 3' ENDS ... EMPLOYING TERMINAL TRANSFERASE ... THE RESULTS ... ESTABLISHED THAT TERMINAL TRANSFERASE ADDED BIOTINATED dUMP TO THE 3' ENDS.") |
| 1600 | | Same as Claim 592 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 592 IS A SEQUENCING DETECTION CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1600 IS FOR A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1601 | | Same as Claim 593 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 593 IS A SEQUENCING DETECTION CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1601 IS FOR A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1602 | | Same as Claim 594 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 594 IS A SEQUENCING DETECTION CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1602 IS FOR A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1603 | | Same as Claim 595 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 595 IS A SEQUENCING DETECTION CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1603 IS FOR A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1604 | | Same as Claim 596 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 596 IS A SEQUENCING DETECTION CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1604 IS FOR A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1605 | 342 | Same as Claim 597 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 597 IS A SEQUENCING DETECTION CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1605 IS FOR A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS |
|---------------|----------------------------------|---|
| | | (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
| 1606 | 343 | Same as Claim 598 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 598 IS A SEQUENCING DETECTION CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1606 IS FOR A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1607 | 344 | Same as Claim 599 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 599 IS A SEQUENCING DETECTION CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1607 IS FOR A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1608 | 345 | <i>ibid.</i> |
| 1609 | 346 | |
| 1610 | 347 | |
| 1611 | 365 | BUT NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 365 WAS A SEQUENCING DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1611 IS FOR A PROCESS FOR PREPARING DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1612 | 366 | BUT NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 366 WAS A SEQUENCING DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1612 IS FOR A PROCESS FOR PREPARING DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1613 | | TO BE ADDRESSED IN A FUTURE RESPONSE. |
| 1614 | | Same as Claim 603 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 603 IS A SEQUENCING DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1614 IS A PROCESS FOR PREPARING DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1615 | | Same as Claim 604 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 604 IS A SEQUENCING DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1615 IS A PROCESS FOR PREPARING DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1616 | | Same as Claim 605 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 605 IS A SEQUENCING DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1616 IS A PROCESS FOR PREPARING DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1617 | | Same as Claim 606 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 606 IS A SEQUENCING DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1617 IS A PROCESS FOR PREPARING DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1618 | | Same as Claim 607 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 607 IS A SEQUENCING DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1618 IS A PROCESS FOR PREPARING DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1619 | 551 | |
| 1620 | 552 | |
| 1621 | | Same as Claim 608 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 608 IS A SEQUENCING DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1621 IS A PROCESS FOR PREPARING DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1622 | | See Claim 609 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 609 IS A SEQUENCING DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1622 IS A PROCESS FOR PREPARING DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1623 | 338 | Former claim 338 recited " . . . Sig is covalently attached to BASE . . . through a linkage group." |
| 1624 | 341 | |
| 1625 | 339 | |
| 1626 | 340 | |
| 1627 | 338 | Former claim 338 also recited " . . . Sig is covalently attached to SM . . . through a linkage group." |
| 1628 | 341 | Same as Claim 1624 above |
| 1629 | 339 | |

| NEW CLAIM NO. | FORMER CLAIM NO. IF APPLICABLE | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|--------------------------------|---|
| 1630 | 340 | |
| 1631 | 338 | Former claim 338 also recited " . . . Sig is covalently attached to SM . . . through a linkage group." |
| 1632 | 341 | Same as Claim 1624 above |
| 1633 | 339 | |
| 1634 | 340 | |
| 1635 | | Same as Claim 612 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 612 IS A SEQUENCING DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1635 IS A PROCESS FOR PREPARING DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1636 | | <i>ibid.</i> |
| 1637 | | Same as Claim 614 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 614 IS A SEQUENCING DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1637 IS A PROCESS FOR PREPARING DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1638 | | Same as Claim 615 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 615 IS A SEQUENCING DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1638 IS A PROCESS FOR PREPARING DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1639 | | Same as Claim 616 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 616 IS A SEQUENCING DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1639 IS A PROCESS FOR PREPARING DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1640 | | Same as Claim 617 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 617 IS A SEQUENCING DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1640 IS A PROCESS FOR PREPARING DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1641 | | Same as Claim 618 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 618 IS A SEQUENCING DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1641 IS A PROCESS FOR PREPARING DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1642 | | Same as Claim 619 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 619 IS A SEQUENCING DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1642 IS A PROCESS FOR PREPARING DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1643 | | Same as Claim 620 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 620 IS A SEQUENCING DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1643 IS A PROCESS FOR PREPARING DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1644 | 338 | |
| 1645 | 339 | |
| 1646 | 340 | |
| 1647 | 341 | |
| 1648 | 285 | Note that New Claim 1648 is directed to a process for preparing a detectable non-radioactively labeled oligo- or polynucleotide, whereas former claim 285 depended from a detection process. |
| 1649 | 531 | NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 531 WAS A DETECTION PROCESS CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1649 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1650 | 532 | NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 532 WAS A DETECTION PROCESS CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1650 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1651 | 533 | NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 533 WAS A DETECTION PROCESS CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1651 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS |
|---------------------|---|--|
| | | (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
| 1652 | 548 | New Claim 1652 recites "wherein said heterocyclic aromatic compound is fluorescent." Former claim 548 recited "wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent." |
| 1653 | 534 | NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 534 WAS A DETECTION PROCESS CLAIM AND THAT THE BASE CLAIM FOR NEW CLAIM 1653 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1654 | 550 | Same as Claim 1652 above |
| 1655 | 286 | Note that former claim 286 was directed to a detection process, whereas New Claim 1655 is directed to a process for preparing a detectable non-radioactively labeled oligo- or polynucleotide. |
| 1656 | 287 | BUT NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 287 WAS DIRECTED TO DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1656 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1657 | 288 | BUT NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 288 WAS DIRECTED TO DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1657 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1658 | 289 | BUT NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 289 WAS DIRECTED TO DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1658 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1659 | 290 | BUT NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 290 WAS DIRECTED TO DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1659 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1660 | 291 | BUT NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 291 WAS DIRECTED TO DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1660 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1661 | 292 | BUT NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 292 WAS DIRECTED TO DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1661 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1662 | 293 | Note that New Claim 1662 is directed to a process for preparing a detectable non-radioactively labeled oligo- or polynucleotide, whereas former claim 293 was directed to a detection process. |
| 1663 | 294 | Note that New Claim 1663 is directed to a process for preparing a detectable non-radioactively labeled oligo- or polynucleotide, whereas former claim 294 was directed to a detection process. |
| 1664 | 295 | Note that New Claim 1664 is directed to a process for preparing a detectable non-radioactively labeled oligo- or polynucleotide, whereas former claim 295 was directed to a detection process. |
| 1665 | 296 | Note that New Claim 1665 is directed to a process for preparing a detectable non-radioactively labeled oligo- or polynucleotide, whereas former claim 296 was directed to a detection process. |
| 1666 | 297 | Note that New Claim 1666 is directed to a process for preparing a detectable non-radioactively labeled oligo- or polynucleotide, whereas former claim 297 was directed to a detection process. |
| 1667 | 298 | Note that New Claim 1667 is directed to a process for preparing a detectable non-radioactively labeled oligo- or polynucleotide, whereas former claim 298 was directed to a detection process. |
| 1668 | 299 | Note that New Claim 1668 is directed to a process for preparing a detectable non-radioactively labeled oligo- or polynucleotide, whereas former claim 299 was directed to a detection process. |
| 1669 | 301 | Note that New Claim 1669 is directed to a process for preparing a detectable non-radioactively labeled oligo- or polynucleotide, whereas former claim 301 was directed to a detection process. |

| NEW CLAIM NO. | FORMER CLAIM NO. IF APPLICABLE | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|--------------------------------|--|
| 1670 | 302 | Note that New Claim 1670 is directed to a process for preparing a detectable non-radioactively labeled oligo- or polynucleotide, whereas former claim 302 was directed to a detection process. |
| 1671 | 385 | Note that former claim 385 was directed to a chromosomal characterization process, whereas New Claim 1671 is directed to a process for preparing a detectable non-radioactively labeled oligo- or polynucleotide of interest. The term "indicator molecule" was also recited in several former dependent claims. See, e.g., former claims 386, 391-392, 401-402 and 404-406. |
| 1672 | | Same as Claim 658 above |
| 1673 | | Same as Claim 659 above |
| 1674 | 548 & 550 | Same as Claims 1652 & 1654 above |
| 1675 | 304 | But note that the base claim for 304 is a detection process and the base claim for claim 1675 is a process for preparing a detectable non-radioactively labeled oligo- or polynucleotide. |
| 1676 | | Same as Claim 1675 above. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 1675. |
| 1677 | 333 | Same as Claim 1386 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1386 IS A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1677 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1678 | | Same as Claim 1379 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1379 IS A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1678 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1679 | 304 | Same as Claim 1675 above |
| 1680 | | Same as Claim 1679 above. NOTE THAT FLUORESCIN IS RECITED AS A MARKUSH MEMBER IN NEW CLAIM 1679. |
| 1681 | | Same as Claim 1340 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1340 IS A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1681 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1682 | 306 | Same as Claim 1383 above BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1383 IS A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1682 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1683 | 287 | Note that "an antibody component" was recited as a Markush member in former claim 287. NOTE FURTHER THAT THE BASE CLAIM FOR FORMER CLAIM 287 WAS A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1683 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1684 | 287 | Note that "a chelating component" was recited as a Markush member in former claim 287. NOTE FURTHER THAT THE BASE CLAIM FOR FORMER CLAIM 287 WAS A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1684 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1685 | 334 | NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 334 WAS A SEQUENCING DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1685 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1686 | 307 | NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 307 WAS A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1686 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1687 | 308 | NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 308 WAS A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1687 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |

Filed: June 7, 1995

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| NEW CLAIM NO. | FORMER CLAIM NO. IF APPLICABLE | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|--------------------------------|--|
| 1688 | 309 | NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 309 WAS A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1688 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1689 | 312 | NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 312 WAS A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1689 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1690 | 313 | NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 313 WAS A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1690 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1691 | 314 | NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 314 WAS A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1691 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1692 | 315 | NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 315 WAS A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1692 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1693 | 316 | NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 316 WAS A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1693 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1694 | 317 | NOTE THAT THE BASE CLAIM FOR FORMER CLAIM 317 WAS A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1694 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1695 | | Same as Claim 1404 above BUT NOTE THAT THE BASE CLAIM FOR CLAIM 1404 IS A DETECTION PROCESS AND THE BASE CLAIM FOR CLAIM 1695 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1696 | 297 | Same as Claim 1405 above BUT NOTE THAT THE BASE CLAIM FOR CLAIM 1405 IS A DETECTION PROCESS AND THE BASE CLAIM FOR CLAIM 1696 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1697 | | Same as Claim 1406 BUT NOTE THAT THE BASE CLAIM FOR CLAIM 1406 IS A DETECTION PROCESS AND THE BASE CLAIM FOR CLAIM 1697 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1698 | | Same as Claim 1409 BUT TO BE ADDRESSED IN PART IN A FUTURE RESPONSE. BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1409 IS A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1698 IS FOR A CHROMOSOMAL CHARACTERIZATION PROCESS. |
| 1699 | | Same as Claim 1297 BUT NOTE THAT THE BASE CLAIM FOR NEW CLAIM 1297 IS A DETECTION PROCESS AND THAT THE BASE CLAIM FOR NEW CLAIM 1570 IS A PROCESS FOR PREPARING A DETECTABLE NON-RADIOACTIVELY LABELED OLIGO- OR POLYNUCLEOTIDE. |
| 1700 | | Same as Claim 569 above EXCEPT FOR TERM "ONE OR MORE CHELATING COMPOUNDS OR CHELATING COMPONENTS" IN "MODIFIED OR LABELED NUCLEOTIDES OR NUCLEOTIDE ANALOGS" AND "DETECTABLE RADIOACTIVE SIGNAL" FOR SUPPORT OF CHELATING COMPOUNDS AND CHELATING COMPONENTS, SEE SPECIFICATION, PAGES 82-85 AND ORIGINAL CLAIMS 169-184 |

| NEW CLAIM NO. | FORMER CLAIM NO. IF APPLICABLE | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------------|---|--|
| 1701 | | Same as Claim 721 above EXCEPT FOR TERM "ONE OR MORE CHELATING COMPOUNDS OR CHELATING COMPONENTS" IN "MODIFIED OR LABELED NUCLEOTIDES OR NUCLEOTIDE ANALOGS" AND "DETECTABLE RADIOACTIVE SIGNAL" FOR SUPPORT OF CHELATING COMPOUNDS AND CHELATING COMPONENTS, SEE SPECIFICATION, PAGES 82-85 AND ORIGINAL CLAIMS 169-184 |
| 1702 | | Same as Claim 873 above EXCEPT FOR TERM ONE OR MORE "CHELATING COMPOUNDS OR CHELATING COMPONENTS" IN "MODIFIED OR LABELED NUCLEOTIDES OR NUCLEOTIDE ANALOGS" AND "DETECTABLE RADIOACTIVE SIGNAL" FOR SUPPORT OF CHELATING COMPOUNDS AND CHELATING COMPONENTS, SEE SPECIFICATION, PAGES 82-85 AND ORIGINAL CLAIMS 169-184 |
| 1703 | | Same as Claim 1025 above EXCEPT FOR TERM "ONE OR MORE CHELATING COMPOUNDS OR CHELATING COMPONENTS" IN "MODIFIED OR LABELED NUCLEOTIDES OR NUCLEOTIDE ANALOGS" AND "DETECTABLE RADIOACTIVE SIGNAL" FOR SUPPORT OF CHELATING COMPOUNDS AND CHELATING COMPONENTS, SEE SPECIFICATION, PAGES 82-85 AND ORIGINAL CLAIMS 169-184 |
| 1704 | | Same as Claim 1177 above EXCEPT FOR TERM "ONE OR MORE CHELATING COMPOUNDS OR CHELATING COMPONENTS" IN "MODIFIED OR LABELED NUCLEOTIDES OR NUCLEOTIDE ANALOGS" AND "DETECTABLE RADIOACTIVE SIGNAL" FOR SUPPORT OF CHELATING COMPOUNDS AND CHELATING COMPONENTS, SEE SPECIFICATION, PAGES 82-85 AND ORIGINAL CLAIMS 169-184 |
| 1705 | | Same as Claim 1298 above EXCEPT FOR TERM "ONE OR MORE CHELATING COMPOUNDS OR CHELATING COMPONENTS" IN "MODIFIED OR LABELED NUCLEOTIDES OR NUCLEOTIDE ANALOGS" AND "DETECTABLE RADIOACTIVE SIGNAL" FOR SUPPORT OF CHELATING COMPOUNDS AND CHELATING COMPONENTS, SEE SPECIFICATION, PAGES 82-85 AND ORIGINAL CLAIMS 169-184 |
| 1706 | | Same as Claim 1411 above EXCEPT FOR TERM "ONE OR MORE CHELATING COMPOUNDS OR CHELATING COMPONENTS" IN "MODIFIED OR LABELED NUCLEOTIDES OR NUCLEOTIDE ANALOGS" AND "DETECTABLE RADIOACTIVE SIGNAL" FOR SUPPORT OF CHELATING COMPOUNDS AND CHELATING COMPONENTS, SEE SPECIFICATION, PAGES 82-85 AND ORIGINAL CLAIMS 169-184 |
| 1707 | | Same as Claim 1473 above EXCEPT FOR TERM "A CHELATING COMPOUND OR CHELATING COMPONENT CAPABLE OF PROVIDING A RADIOACTIVE SIGNAL" FOR "SIG IS A SIGNALING MOIETY COMPRISING . . ." AND "RADIOACTIVELY" DETECTING. FOR SUPPORT OF CHELATING COMPOUNDS AND CHELATING COMPONENTS, SEE SPECIFICATION, PAGES 82-85 AND ORIGINAL CLAIMS 169-184 |
| 1708 | | Same as Claim 1474 above EXCEPT FOR TERM "A CHELATING COMPOUND OR CHELATING COMPONENT CAPABLE OF PROVIDING A RADIOACTIVE SIGNAL" FOR "SIG IS A SIGNALING MOIETY COMPRISING . . ." AND "RADIOACTIVELY" DETECTING. FOR SUPPORT OF CHELATING COMPOUNDS AND CHELATING COMPONENTS, SEE SPECIFICATION, PAGES 82-85 AND ORIGINAL CLAIMS 169-184 |
| 1709 | | Same as Claim 1475 above EXCEPT FOR TERM "A CHELATING COMPOUND OR CHELATING COMPONENT CAPABLE OF PROVIDING A RADIOACTIVE SIGNAL" FOR "SIG IS A SIGNALING MOIETY COMPRISING . . ." AND "RADIOACTIVELY" DETECTING. FOR SUPPORT OF CHELATING COMPOUNDS AND CHELATING COMPONENTS, SEE SPECIFICATION, PAGES 82-85 AND ORIGINAL CLAIMS 169-184 |
| 1710 | | Same as Claim 1476 above EXCEPT FOR TERM "A CHELATING COMPOUND OR CHELATING COMPONENT CAPABLE OF PROVIDING A RADIOACTIVE SIGNAL" FOR "SIG IS A SIGNALING MOIETY COMPRISING . . ." AND "RADIOACTIVELY" DETECTING. FOR SUPPORT OF CHELATING COMPOUNDS AND CHELATING COMPONENTS, SEE SPECIFICATION, PAGES 82-85 AND ORIGINAL CLAIMS 169-184 |

| NEW CLAIM NO. | FORMER CLAIM NO. IF APPLICABLE | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------------|---|---|
| 1711 | | Same as Claim 1582 above EXCEPT FOR TERM "A CHELATING COMPOUND OR CHELATING COMPONENT CAPABLE OF PROVIDING A RADIOACTIVE SIGNAL" FOR "SIG IS A SIGNALING MOIETY COMPRISING . . ." AND "RADIOACTIVELY" DETECTING. FOR SUPPORT OF CHELATING COMPOUNDS AND CHELATING COMPONENTS, SEE SPECIFICATION, PAGES 82-85 AND ORIGINAL CLAIMS 169-184 |
| 1712 | | Specification, Page 84, 2nd ¶ ("This type of self-signaling molecule can be used to monitor any nucleic acid hybridization reaction. It is particularly important for detecting nucleic acids in gels (for example, sequencing gels.)" Specification, Page 89, 1st full ¶ ("Another aspect of the practices of this invention is to carry out the detection or hybridization in the liquid phase between the DNA sought to be detected and the DNA detecting probe. In this liquid phase detection system both the DNA molecule to be detected and the appropriate DNA detecting probe are not attached to any insoluble substrate or any insoluble chemical moiety.") Specification, Page 98, 2nd ¶ ("... A probe having a desired nucleotide sequence, such as a single-stranded polynucleotide, either DNA or RNA probe, would then be brought into contact with DNA or RNA genetic material to be identified. Upon localization of the probe and formation of a double-stranded polynucleotide containing the probe and the matching DNA or RNA material to be identified, the resulting formed double-stranded DNA or RNA-containing material would then be observable and identified.") |
| 1713 | | Specification, Page 90, 2nd ¶ ("... After hybridization, excess non-hybridized probe DNA would be digested with S1 nuclease and exonuclease I . . .") |
| 1714 | | Same as Claim 1299 above |
| 1715 | | <i>ibid.</i> |
| 1716 | 287 | SEE ALSO SPECIFICATION, PAGE 96, LAST ¶, THROUGH PAGE 97, 1ST ¶ ("THE SIG MOIETY EMPLOYED . . . COULD INCLUDE . . .") |

| NEW CLAIM NO. | FORMER CLAIM NO. (IF APPLICABLE) | COMMENTS (ADDITIONAL LANGUAGE IN NEW CLAIM(S), SUPPORT IN SPECIFICATION, ORIGINAL CLAIMS, ETC.) |
|---------------|----------------------------------|---|
| 1717 | 369 | <p><u>Support for direct detection</u></p> <p>Specification, Page 93, lines 18-25 ("... The Sig moiety is covalently attached ... and when so attached is capable of signalling itself or makes itself self-detecting or its presence known ...")</p> <p>Specification, Page 94, lines 7-11 ("The Sig chemical moiety is covalently attached ... and said Sig chemical moiety when attached ... is capable of signalling itself or making itself self-detecting or its presence known ...")</p> <p>Specification, Page 95, lines 10-12 ("... said Sig, when attached to said P moiety being capable of signalling itself or making itself self-detecting or its presence known ...")</p> <p>Specification, Page 95, last five lines ("The resulting nucleotides containing the Sig moiety attached thereto are capable of signalling themselves or making themselves self-detecting or their presence known and being detectable ...")</p> <p>SEE ALSO FORMER CLAIM 369 WHICH RECITED "WHEREIN SAID DETECTING STEP IS CARRIED OUT DIRECTLY" AND DEPENDED FROM FORMER CLAIM 348 (A SEQUENCING CLAIM).</p> <p><u>Support for Indirect Detection</u></p> <p>Page 6, Penultimate ¶ ("These various utilities are based upon the ability of the molecules to form stable complexes with polypeptides which in turn can be detected, either by means of properties inherent in the polypeptide or by means of detectable moieties which are attached to, or which interact with, the polypeptide.")</p> <p>Page 7, last three lines, through Page 8, 1st two lines ("... it is preferable that the probe moiety be attached ... so that it can readily interact with antibodies, other detector proteins, or chemical reagents.")</p> <p>Page 25, penultimate ¶, through Page 26, 1st ¶ ("The various modified nucleotides, oligonucleotides, and polynucleotides of this invention may be detected by contacting the compounds with polypeptides ... [which] include one or more moieties which can be detected ... One polypeptide detector for the biotinyl-type probe is avidin. ... If avidin is coupled to potentially demonstrable indicator molecules, ...")</p> <p>Page 26, last ¶, through Page 27, 1st ¶ ("A most preferred protein for biotin-like probe detection is monospecific rabbit IgG, anti-biotin immunoglobulin. ... anti-biotin antibodies have proven extremely useful in detecting specific polynucleotide sequences on chromosomes ...")</p> <p>Page 30, 1st & 2nd ¶ ("... Hybridized nucleic acid duplexes are then identified by forming a complex between the duplex and a suitable polypeptide which carries a detectable moiety. ... can be detected following hybridization with a polynucleotide probe according to this invention based upon complex formation with a suitable detectable polypeptide.")</p> <p>Page 31, last line, through Page 32, 1st line ("... as detected by indirect immunofluorescence for <u>in situ</u> mapping.")</p> <p>Page 33, 1st full ¶ ("indirect immunofluorescence")</p> <p>Page 36, last ¶ ("An alternative to the fluorescence method for visualizing hybridized probes is to direct enzymes such as peroxidase, alkaline phosphatase or (sic) β-galactosidase to the hybridization site where enzymatic conversion of soluble substrates to insoluble colored precipitates permits light microscope visualization.")</p> <p>Page 38, 1st ¶ ("These polynucleotides are hybridized ... and the resulting duplexes contacted with appropriate polypeptides ... [which] include detectable moieties ...")</p> |
| 1718 | 287 | <p>Same as Claim 1716 above BUT NOTE THAT THE MARKUSH MEMBERS IN CLAIM 1718 ARE RECITED AS MEASUREMENTS AND NOT AS COMPONENTS. BUT SEE FORMER CLAIM 334 ("... A FLUORESCENT MEASUREMENT AND A CHEMILUMINESCENT MEASUREMENT, ...")</p> |

569. (Amended) A process for determining the sequence of a nucleic acid of interest, comprising the steps of:

providing or generating detectable labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said one or more modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety, or the base analog thereof;

subjecting said detectable labeled fragments to a sequencing gel to separate or resolve said fragments; and

detecting non-radioactively the presence of each of said separated or resolved fragments by means of said modified or labeled nucleotides or nucleotide analogs, and determining the sequence of said nucleic acid of interest.

-- 570. (NEW) The process according to claim 569, wherein the nucleic acid sequence of interest is derived from an organism. --

-- 571. (NEW) The process according to claim 570, wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing. --

-- 572. (NEW) The process according to claim 571, wherein said organism comprises a mammal. --

-- 573. (NEW) The process according to claim 572, wherein said mammal comprises a human being. --

-- 574. (NEW) The process according to claim 570, wherein said organism is living. --

-- 575. (NEW) The process according to claims 570 or 574, wherein said organism is selected from the group consisting of prokaryotes and eukaryotes. --

-- 576. (NEW) The process according to claim 575, wherein said organism comprises a eukaryote. --

- 577. (NEW) The process according to claim 576, wherein said eukaryotic nucleic acid sequence of interest is contained within a chromosome. --
- 578. (NEW) The process according to claim 576, wherein said eukaryote comprises a mammal. --
- 579. (NEW) The process according to claim 578, wherein said mammalian nucleic acid sequence of interest is contained within a chromosome. --
- 580. (NEW) The process according to claim 578, wherein said mammal comprises a human being. --
- 581. (NEW) The process according to claim 580, wherein said human nucleic acid sequence of interest is contained within a chromosome. --
- 582. (NEW) The process according to claim 581, wherein said human chromosomal nucleic acid sequence of interest is part of a human gene library. --
- 583. (NEW) The process according to claim 569, wherein said providing or generating step is carried out by means of one or more primers or nucleoside triphosphates or analogs thereof. --
- 584. (NEW) The process according to claim 583, wherein said nucleoside triphosphates are selected from the group consisting of ribonucleoside triphosphates, deoxyribonucleoside triphosphates, dideoxyribonucleoside triphosphates, and analogs of any of the foregoing. --
- 585. (NEW) The process according to claim 569, wherein said fragments have been obtained or generated by a nucleic acid sequencing step or technique. --
- 586. (Amended) The process according to claim 569, wherein the detectable labeled complementary nucleic acid is fragmented prior to separation in said sequencing gel.

-- 587. (NEW) The process according to claim 569, wherein said providing or generating step, the one or more modified or labeled nucleotides or nucleotide analogs have been incorporated into said nucleic acid fragment or fragments. --

-- 588. (NEW) The process according to claim 587, wherein at least one of said modified or labeled nucleotides or nucleotide analogs is at a terminus of said fragment or fragments. --

-- 589. (NEW) The process according to claim 588, wherein said terminus comprises the 5' or the 3' terminus. --

-- 590. (NEW) The process according to claim 587, wherein said incorporation has been carried out in the presence of a primer. --

-- 591. (NEW) The process according to claim 569, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme. --

-- 592. (NEW) The process according to claim 591, wherein said enzyme comprises terminal transferase. --

-- 593. (NEW) The process according to claim 569, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling. --

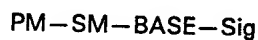
594. (Wholly Rewritten) The process according to claim 593, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.

-- 595. (NEW) The process according to claim 593, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase. --

-- 596. (NEW) The process according to claim 569, wherein said incorporation comprises nick translation. --

- 597. (NEW) The process according to claim 569 or 596, wherein said incorporation is carried out by means of a polymerizing enzyme. --
- 598. (NEW) The process according to claim 597, wherein said polymerizing enzyme comprises a polymerase. --
- 599. (NEW) The process according to claim 598, wherein said polymerase is, selected from the group consisting of DNA polymerase and RNA polymerase. --
- 600. (NEW) The process according to claim 569, wherein said providing or generating step, the modified or labeled nucleotides or nucleotide analogs comprise one or more members selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

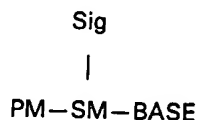
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety or a base analog of any of the foregoing; and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

- (ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

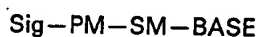
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety, and

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog, said nucleotide having the formula



wherein

PM is a phosphate moiety or phosphate analog,

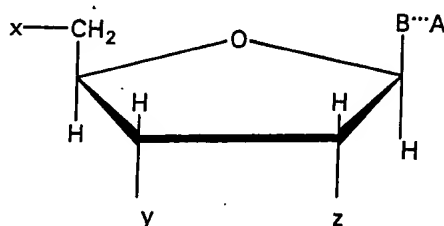
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
Sig is covalently attached to PM directly or through a linkage group. --

-- 601. (NEW) The process according to claim 569, wherein said providing or
generating step, the modified or labeled nucleotides or nucleotide analogs have the
structure:



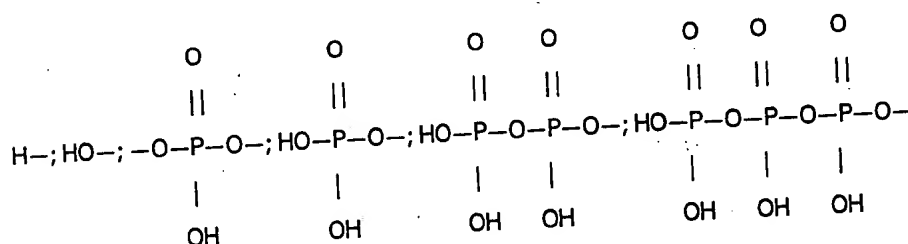
wherein B represents a purine moiety, a 7-deazapurine moiety, a pyrimidine moiety, or an analog of any of the foregoing, and B is covalently bonded to the C1' position of the sugar moiety or sugar analog, provided that whenever B is a purine, a purine analog, a 7-deazapurine moiety or a 7-deazapurine analog, the sugar moiety or sugar analog is attached at the N9 position of the purine moiety, the purine analog, the 7-deazapurine moiety or the 7-deazapurine analog thereof, and

whenever B is a pyrimidine moiety or a pyrimidine analog, the sugar moiety or sugar analog is attached at the N1 position of the pyrimidine moiety or the pyrimidine analog;

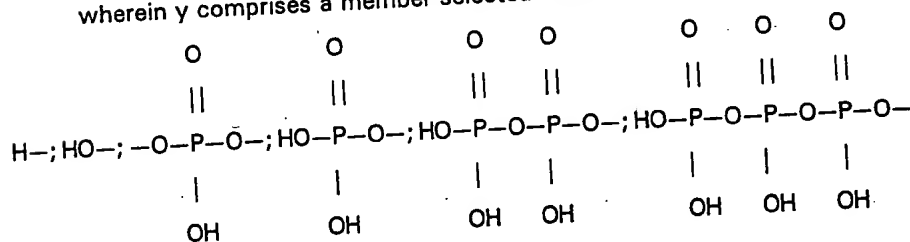
wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal; and

wherein B and A are covalently attached directly or through a linkage group, wherein if B is a purine or a purine analog, A is attached to the 8-position of the purine or purine analog, if B is a 7-deazapurine or 7-deazapurine analog, A is attached to the 7-position of the deazapurine or deazapurine analog, and if B is a pyrimidine or a pyrimidine analog, A is attached to the 5-position of the pyrimidine or pyrimidine analog; and

wherein x comprises a member selected from the group consisting of:



wherein y comprises a member selected from the group consisting of:



wherein z comprises a member selected from the group consisting of H- and HO-.

-- 602. (NEW) The process according to claim 601, wherein y and z comprise H-.

-- 603. (NEW) The process according to claim 569, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a mono-phosphate, a di-phosphate, a tri-phosphate and a tetra-phosphate.

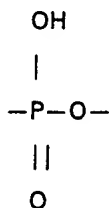
- 604. (NEW) The process according to claim 600, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise a nucleoside mono-, di- or tri-phosphate. --
- 605. (NEW) The process according to claims 569 or 600, wherein said sugar moiety or sugar analog comprises a monosaccharide. --
- 606. (NEW) The process according to claim 605, wherein said monosaccharide comprises a furanose. --
- 607. (NEW) The process according to claim 606, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose. --
- 608. (NEW) The process according to claim 600, wherein said base moiety or base analog BASE in any of said nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --
- 609. (NEW) The process according to claim 600, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --
- 610. (NEW) The process according to claim 600, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to BASE at a position when BASE is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof. --

-- 611. (NEW) The process according to claim 600, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position selected from the group consisting of the N⁴ position when said pyrimidine comprises cytosine, the N² position when said purine comprises adenine or deazaadenine, the N⁶ position when said purine comprises guanine or deazaguanine, and combinations thereof. --

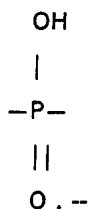
-- 612. (NEW) The process according to claim 606, wherein in said nucleotide (ii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 613. (NEW) The process according to claim 606, wherein in said nucleotide (iii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 614 (NEW) The process according to claim 600, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



and



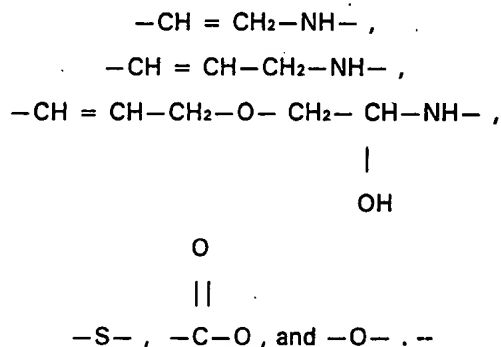
-- 615. (NEW) The process according to claim 600, wherein PM is a mono-, di- or tri-phosphate, and wherein in said nucleotide or nucleotide analog (iii), the Sig moiety is covalently attached to PM through a phosphorus or phosphate oxygen. --

-- 616. (NEW) The process according to claim 600, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal. --

-- 617. (NEW) The process according to claim 600, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $\text{--CH}_2\text{NH--}$ moiety, or both. --

-- 618. (NEW) The process according to claim 600, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group. --

-- 619. (NEW) The process according to claim 600, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



-- 620. (NEW) The process according to claim 600, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety. --

-- 621. (NEW) The process according to claim 600, wherein in any of said nucleotides or nucleotide analogs (i), (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group. --

-- 622. (NEW) The process according to claim 621, wherein said linkage group contains an amine. --

-- 623. (NEW) The process according to claim 622, wherein said amine comprises a primary amine. --

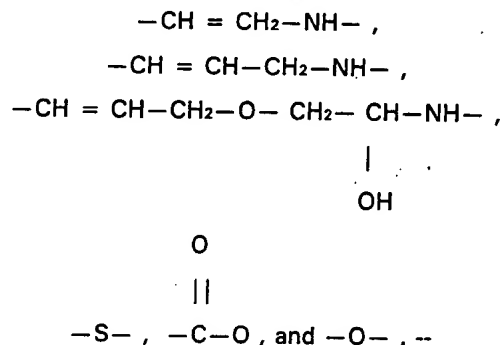
-- 624. (NEW) The process according to claim 621, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable signal. --

-- 625. (NEW) The process according to claim 601, wherein said covalent attachment does not interfere substantially with the characteristic ability of A to form a detectable non-radioactive signal. --

-- 626. (NEW) The process according to claim 601, wherein said covalent attachment comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $-\text{CH}_2\text{NH}-$ moiety, or both. --

--627. (NEW) The process according to claim 601, wherein said covalent attachment comprises an allylamine group. --

-- 628. (NEW) The process according to claim 601, wherein said covalent attachment comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



-- 629. (NEW) The process according to claim 601, wherein said covalent attachment includes a glycosidic linkage moiety. --

-- 630. (NEW) The process according to claim 601, wherein said A is covalently attached to B through a linkage group. --

-- 631. (NEW) The process according to claim 630, wherein said linkage group contains an amine. --

-- 632. (NEW) The process according to claim 631, wherein said amine comprises a primary amine. --

-- 633. (NEW) The process according to claim 630, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal. --

- 634. (NEW) The process according to claim 600, wherein Sig comprises at least three carbon atoms. --
- 635. (NEW) The process according to claim 600, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --
- 636. (NEW) The process according to claim 600, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms. --
- 637. (NEW) The process according to claim 600, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic moiety comprising at least five carbon atoms. --
- 638. (NEW) The process according to claim 637, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent. --
- 639. (NEW) The process according to claim 600, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --
- 640. (NEW) The process according to claim 639, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent. --
- 641. (NEW) The process according to claim 600, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide. --
- 642. (NEW) The process according to claim 600, wherein Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --
- 643. (NEW) The process according to claim 642, wherein Sig comprises an electron dense component. --

-- 644. (NEW) The process according to claim 643, wherein said electron dense component comprises ferritin. --

-- 645. (NEW) The process according to claim 642, wherein Sig comprises a magnetic component. --

-- 646. (NEW) The process according to claim 645, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --

-- 647. (NEW) The process according to claim 645, wherein said magnetic component comprises magnetic beads. --

-- 648. (NEW) The process according to claim 600, wherein Sig comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein. --

-- 649. (NEW) The process according to claim 648, wherein the binding protein comprises a lectin. --

-- 650. (NEW) The process according to claim 649, wherein the lectin comprises concanavalin A. --

-- 651. (NEW) The process according to claim 649, wherein said lectin is conjugated to ferritin. --

-- 652. (NEW) The process according to claim 642, wherein Sig comprises an enzyme. --

-- 653. (NEW) The process according to claim 652, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, β -galactosidase, ribonuclease, glucose oxidase, peroxidase, and a combination thereof. --

-- 654. (NEW) The process according to claim 642, wherein Sig comprises a hormone. --

-- 655. (NEW) The process according to claim 642, wherein Sig comprises a metal-containing component. --

-- 656. (NEW) The process according to claim 655, wherein said metal-containing component is catalytic. --

-- 657. (NEW) The process according to claim 600, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule. --

-- 658. (NEW) The process according to claim 657, wherein said indicator molecule comprises an aromatic compound. --

-- 659. (NEW) The process according to claim 658, wherein said aromatic compound is heterocyclic. --

-- 660. (NEW) The process according to claim 659, wherein said heterocyclic aromatic compound is fluorescent. --

-- 661. (NEW) The process according to claim 660, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing. --

-- 662. (NEW) The process according to claim 661, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --

-- 663. (NEW) The process according to claim 642, wherein Sig comprises a fluorescent component. --

-- 664. (NEW) The process according to claim 663, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --

-- 665. (NEW) The process according to claim 664, wherein said fluorescent component comprises fluorescein. --

- 666. (NEW) The process according to claim 642, wherein Sig comprises a chemiluminescent component. --
- 667. (NEW) The process according to claim 642, wherein Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component. --
- 668. (NEW) The process according to claim 642, wherein Sig comprises an antibody component. --
- 669. (NEW) The process according to claim 642, wherein Sig comprises a chelating component. --
- 670. (NEW) The process according to claim 657, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing. --
- 671. (NEW) The process according to claim 601, wherein A comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --
- 672. (NEW) The process according to claim 601, wherein A comprises an aliphatic chemical moiety comprising at least four carbon atoms. --
- 673. (NEW) The process according to claim 601, wherein A comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms. --
- 674. (NEW) The process according to claim 673, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent. --
- 675. (NEW) The process according to claim 601, wherein A comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --
- 676. (NEW) The process according to claim 675, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent. --

- 677. (NEW) The process according to claim 601, wherein A comprises a monosaccharide, polysaccharide or an oligosaccharide. --
- 678. (NEW) The process according to claim 601, wherein A comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-, containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --
- 679. (NEW) The process according to claim 678, wherein A comprises an electron dense component. --
- 680. (NEW) The process according to claim 679, wherein said electron dense component comprises ferritin. --
- 681. (NEW) The process according to claim 680, wherein A comprises a magnetic component. --
- 682. (NEW) The process according to claim 681, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --
- 683. (NEW) The process according to claim 681, wherein said magnetic component comprises magnetic beads. --
- 684. (NEW) The process according to claim 601, wherein A comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein. --
- 685. (NEW) The process according to claim 684, wherein the binding protein comprises a lectin. --
- 686. (NEW) The process according to claim 685, wherein the lectin comprises concanavalin A. --

- 687. (NEW) The process according to claim 685, wherein said lectin is conjugated to ferritin. --
- 688. (NEW) The process according to claim 678, wherein A comprises an enzyme. --
- 689. (NEW) The process according to claim 688, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, β -galactosidase, ribonuclease, glucose oxidase, peroxidase, and a combination thereof. --
- 690. (NEW) The process according to claim 678, wherein A comprises a hormone. --
- 691. (NEW) The process according to claim 678, wherein A comprises a metal-containing component. --
- 692. (NEW) The process according to claim 691, wherein said metal-containing component is catalytic. --
- 693. (NEW) The process according to claim 601, wherein said A comprises an indicator molecule. --
- 694. (NEW) The process according to claim 693, wherein said indicator molecule comprises an aromatic compound. --
- 695. (NEW) The process according to claim 694, wherein said aromatic compound is heterocyclic. --
- 696. (NEW) The process according to claim 695, wherein said heterocyclic aromatic compound is fluorescent. --
- 697. (NEW) The process according to claim 696, wherein said fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing. --

- 698. (NEW) The process according to claims 696 or 697, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --
- 699. (NEW) The process according to claim 678, wherein A comprises a fluorescent component. --
- 700. (NEW) The process according to claim 699, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --
- 701. (NEW) The process according to claim 700, wherein said fluorescent component comprises fluorescein. --
- 702. (NEW) The process according to claim 678, wherein A comprises a chemiluminescent component. --
- 703. (NEW) The process according to claim 678, wherein A comprises an antigenic or hapten component capable of complexing with an antibody specific to the component. --
- 704. (NEW) The process according to claim 678, wherein A comprises an antibody component. --
- 705. (NEW) The process according to claim 678, wherein A comprises a chelating component. --
- 706. (NEW) The process according to claim 693, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing. --
- 707. (NEW) The process according to claim 569, wherein said labeled nucleic acid fragments are detectable by a non-radioactive means selected from the group consisting of a fluorescent measurement, a chemiluminescent measurement, and a combination thereof. --

- 708. (NEW) The process according to claim 569, wherein said subjecting step is carried out electrophoretically. --
- 709. (NEW) The process according to claims 569, 600 or 601, wherein said detecting step is carried out directly. --
- 710. (NEW) The process according to claim 709, wherein said direct detection is carried out using one or more indicator molecules. --
- 711. (NEW) The process according to claim 710, wherein said one or more indicator molecules comprise fluoresceinated nucleotides or nucleotide analogs. --
- 712. (NEW) The process according to claim 711, wherein said fluoresceinated nucleotides or nucleotide analogs comprise fluoresceinated DNA. --
- 713. (NEW) The process according to claim 709, wherein said detecting step is carried out by means of a directly detectable signal provided by said one or more modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety. --
- 714. (NEW) The process according to claim 713, wherein in said detecting step the directly detectable signal comprises a member selected from the group consisting of a chelating compound, a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound and an electron dense compound. --
- 715. (NEW) The process according to claim 713, wherein in said detecting step the directly detectable signal providing Sig detectable non-radioactive moiety comprises an enzyme. --
- 716. (Amended) The process according to claims 569, 600 or 601, wherein said detecting step is carried out by means of an indirectly detectable signal provided by said one or more modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

-- 717. (NEW) The process according to claim 716, wherein in said detecting step the indirectly detectable signal is selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme. --

~~DELETED PER 2ND SUPPL. AMEND. 8/31/00 -- 718. (NEW) The process according to claim 717, wherein in said detecting step the indirectly detectable signal is provided by a polynucleotide sequence capable of recognizing a signal containing moiety.~~

719. (Wholly Rewritten) The process according to claim 569, wherein said modified or labeled nucleotides or nucleotide analogs are capable of being detected non-radioactively by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a phosphorescent measurement, a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

-- 720. (NEW) The process according to claim 569, wherein said detecting step comprises localizing said labeled nucleic acid fragments by means of said modified or labeled nucleotides or nucleotide analogs. --

721. (Amended) A process for determining the sequence of a nucleic acid of interest, comprising the steps of:

providing or generating detectable labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said one or more modified nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety, or the base analog thereof;

introducing or subjecting said detectable labeled fragments to a sequencing gel;

separating or resolving said fragments in said sequencing gel; and

detecting non-radioactively each of the separated or resolved fragments; and determining the sequence of said nucleic acid of interest.

- 722. (NEW) The process according to claim 721, wherein the nucleic acid sequence of interest is derived from an organism. --
- 723. (NEW) The process according to claim 722, wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing. --
- 724. (NEW) The process according to claim 723, wherein said organism comprises a mammal. --
- 725. (NEW) The process according to claim 724, wherein said mammal comprises a human being. --
- 726. (NEW) The process according to claim 721, wherein said organism is living. --
- 727. (NEW) The process according to claims 722 or 726, wherein said organism is selected from the group consisting of prokaryotes and eukaryotes. --
- 728. (NEW) The process according to claim 727, wherein said organism comprises a eukaryote. --
- 729. (NEW) The process according to claim 728, wherein said eukaryotic nucleic acid sequence of interest is contained within a chromosome. --
- 730. (NEW) The process according to claim 728, wherein said eukaryote comprises a mammal. --
- 731. (NEW) The process according to claim 730, wherein said mammalian nucleic acid sequence of interest is contained within a chromosome. --
- 732. (NEW) The process according to claim 730, wherein said mammal comprises a human being. --

-- 733. (NEW) The process according to claim 732, wherein said human nucleic acid sequence of interest is contained within a chromosome. --

--734. (NEW) The process according to claim 733, wherein said human chromosomal nucleic acid sequence of interest is part of a human gene library. --

-- 735. (NEW) The process according to claim 721, wherein said providing or generating step is carried out by means of one or more primers or nucleoside triphosphates or analogs thereof. --

-- 736. (NEW) The process according to claim 735, wherein said nucleoside triphosphates are selected from the group consisting of ribonucleoside triphosphates, deoxyribonucleoside triphosphates, dideoxyribonucleoside triphosphates, and analogs of any of the foregoing. --

-- 737. (NEW) The process according to claim 721, wherein said fragments have been obtained or generated by a nucleic acid sequencing step or technique. --

738. (Amended) The process according to claim 721, wherein the detectable labeled complementary nucleic acid is fragmented prior to separation in said sequencing gel.

-- 739. (NEW) The process according to claim 721, wherein said providing or generating step, the one or more modified or labeled nucleotides or nucleotide analogs have been incorporated into said nucleic acid fragment or fragments. --

-- 740. (NEW) The process according to claim 739, wherein at least one of said modified or labeled nucleotides or nucleotide analogs is at a terminus of said fragment or fragments. --

-- 741. (NEW) The process according to claim 740, wherein said terminus comprises the 5' or the 3' terminus. --

-- 742. (NEW) The process according to claim 739, wherein said incorporation has been carried out in the presence of a primer. --

-- 743. (NEW) The process according to claim 721, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme. --

-- 744. (NEW) The process according to claim 743, wherein said enzyme comprises terminal transferase. --

-- 745. (NEW) The process according to claim 721, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling. --

746. (Wholly Rewritten) The process according to claim 745, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.

-- 747. (NEW) The process according to claim 745, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase. --

-- 748. (NEW) The process according to claim 721, wherein said incorporation comprises nick translation. --

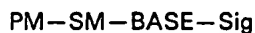
--749. (NEW) The process according to claim 721 or 748, wherein said incorporation is carried out by means of a polymerizing enzyme. --

-- 750. (NEW) The process according to claim 749, wherein said polymerizing enzyme comprises a polymerase. --

-- 751. (NEW) The process according to claim 750, wherein said polymerase is selected from the group consisting of DNA polymerase and RNA polymerase. --

-- 752. (NEW) The process according to claim 721, wherein said providing or generating step, the modified or labeled nucleotides or nucleotide analogs comprise one or more members selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

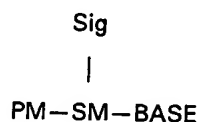
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety
or a base analog of any of the foregoing; and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
Sig is covalently attached to BASE directly or through a linkage group at a position
other than the C5 position when BASE is a pyrimidine moiety or an analog thereof,
at a position other than the C8 position when BASE is a purine moiety or an analog
thereof and at a position other than the C7 position when BASE is a 7-deazapurine
moiety or an analog thereof;

(ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

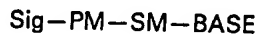
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog, said nucleotide having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

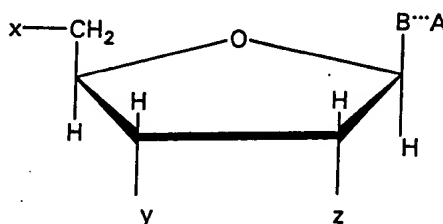
BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
Sig is covalently attached to PM directly or through a linkage group. --

-- 753. (NEW) The process according to claim 721, wherein in said providing or
generating step, the modified or labeled nucleotides or nucleotide analogs have the
structure:

(i)

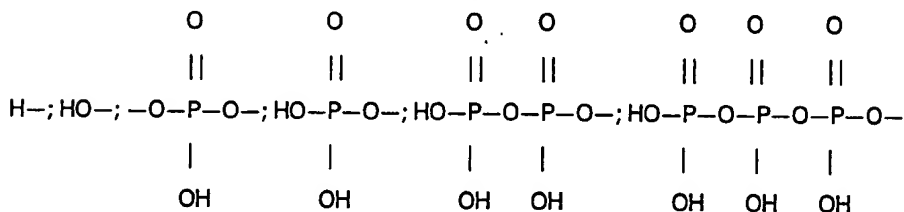


wherein B represents a purine moiety, a 7-deazapurine moiety, a pyrimidine moiety, or an analog of any of the foregoing, and B is covalently bonded to the C1'-position of the sugar moiety or sugar analog, provided that whenever B is a purine, a purine analog, a 7-deazapurine moiety or a 7-deazapurine analog, the sugar moiety or sugar analog is attached at the N9 position of the purine moiety, the purine analog, the 7-deazapurine moiety or the 7-deazapurine analog thereof, and whenever B is a pyrimidine moiety or a pyrimidine analog, the sugar moiety or sugar analog is attached at the N1 position of the pyrimidine moiety or the pyrimidine analog;

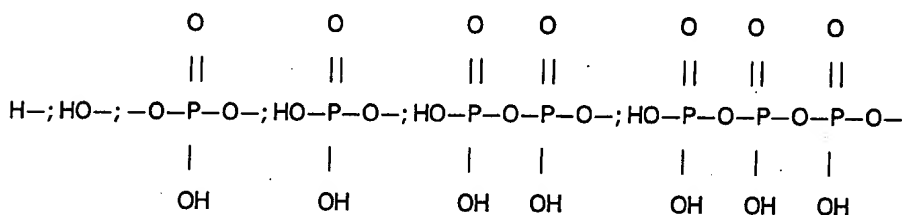
wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal; and

wherein B and A are covalently attached directly or through a linkage group,
wherein if B is a purine or a purine analog, A is attached to the 8-position of the purine or purine analog, if B is a 7-deazapurine or 7-deazapurine analog, A is attached to the 7-position of the deazapurine or deazapurine analog, and if B is a pyrimidine or a pyrimidine analog, A is attached to the 5-position of the pyrimidine or pyrimidine analog; and

wherein x comprises a member selected from the group consisting of:



wherein y comprises a member selected from the group consisting of:



wherein z comprises a member selected from the group consisting of H- and HO- -- .

-- 754. (NEW) The process according to claim 753, wherein y and z comprise H. --

-- 755. (NEW) The process according to claim 721, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a mono-phosphate, a di-phosphate, a tri-phosphate and a tetra-phosphate. --

-- 756. (NEW) The process according to claim 752, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise a nucleoside mono-, di- or tri-phosphate. --

-- 757. (NEW) The process according to claims 721 or 752, wherein said sugar moiety or sugar analog comprises a monosaccharide. --

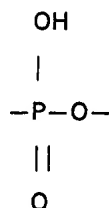
-- 758. (NEW) The process according to claim 757, wherein said monosaccharide comprises a furanose. --

-- 759. (NEW) The process according to claim 758, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose. --

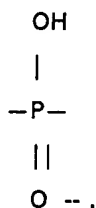
- 760. (NEW) The process according to claim 752, wherein said base moiety or base analog BASE in any of said nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --
- 761. (NEW) The process according to claim 752, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --
- 762. (NEW) The process according to claim 752, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to BASE at a position when BASE is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof. --
- 763. (NEW) The process according to claim 752, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position selected from the group consisting of the N⁴ position when said pyrimidine comprises cytosine, the N² position when said purine comprises adenine or deazaadenine, the N⁶ position when said purine comprises guanine or deazaguanine, and combinations thereof. --
- 764. (NEW) The process according to claim 758, wherein in said nucleotide (ii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 765. (NEW) The process according to claim 758, wherein in said nucleotide (iii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 766. (NEW) The process according to claim 752, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



and



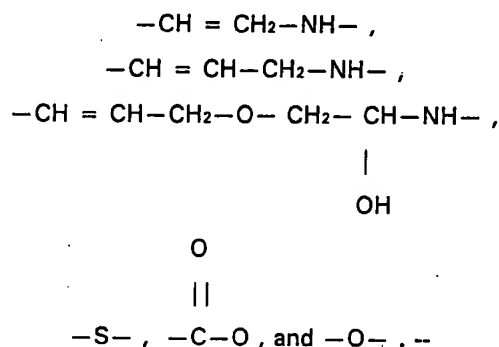
-- 767. (NEW) The process according to claim 752, wherein PM is a mono-, di or tri-phosphate, and wherein said nucleotide or nucleotide analog (iii), the Sig moiety is covalently attached to PM through a phosphorus or phosphate oxygen. --

--768. (NEW) The process according to claim 752, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal. --

-- 769. (NEW) The process according to claim 752, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $\text{--CH}_2\text{NH--}$ moiety, or both. --

-- 770. (NEW) The process according to claim 752, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group. --

-- 771. (NEW) The process according to claim 752, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



-- 772. (NEW) The process according to claim 752, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety. --

--773. (NEW) The process according to claim 752, wherein in any of said nucleotides or nucleotide analogs (i), (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group. --

-- 774. (NEW) The process according to claim 773, wherein said linkage group contains an amine. --

--775. (NEW) The process according to claim 774, wherein said amine comprises a primary amine. --

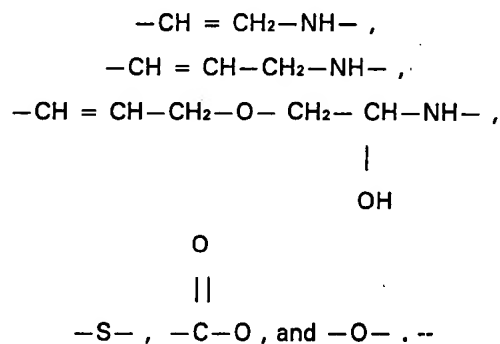
-- 776. (NEW) The process according to claim 773, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable signal. --

-- 777. (NEW) The process according to claim 753, wherein said covalent attachment does not interfere substantially with the characteristic ability of A to form a detectable non-radioactive signal. --

-- 778. (NEW) The process according to claim 753, wherein said covalent attachment comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $-\text{CH}_2\text{NH}-$ moiety, or both. --

-- 779. (NEW) The process according to claim 753, wherein said covalent attachment comprises an allylamine group. --

--780. (NEW) The process according to claim 753, wherein said covalent attachment comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



-- 781. (NEW) The process according to claim 753, wherein said covalent attachment includes a glycosidic linkage moiety. --

-- 782. (NEW) The process according to claim 753, wherein said A is covalently attached to B through a linkage group. --

-- 783. (NEW) The process according to claim 782, wherein said linkage group contains an amine. --

-- 784. (NEW) The process according to claim 783, wherein said amine comprises a primary amine. --

- 785. (NEW) The process according to claim 782, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal. --
- 786. (NEW) The process according to claim 752, wherein Sig comprises at least three carbon atoms. --
- 787. (NEW) The process according to claim 752, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --
- 788. (NEW) The process according to claim 752, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms. --
- 789. (NEW) The process according to claim 752, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic moiety comprising at least five carbon atoms. --
- 790. (NEW) The process according to claim 789, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent. --
- 791. (NEW) The process according to claim 752, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --
- 792. (NEW) The process according to claim 791, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent. --
- 793. (NEW) The process according to claim 752, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide. --

- 794. (NEW) The process according to claim 752, wherein Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --
- 795. (NEW) The process according to claim 794, wherein Sig comprises an electron dense component. --
- 796. (NEW) The process according to claim 795, wherein said electron dense component comprises ferritin. --
- 797. (NEW) The process according to claim 794, wherein Sig comprises a magnetic component. --
- 798. (NEW) The process according to claim 797, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --
- 799. (NEW) The process according to claim 797, wherein said magnetic component comprises magnetic beads. --
- 800. (NEW) The process according to claim 752, wherein Sig comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein. --
- 801. (NEW) The process according to claim 800, wherein the binding protein comprises a lectin. --
- 802. (NEW) The process according to claim 801, wherein the lectin comprises concanavalin A. --
- 803. (NEW) The process according to claim 801, wherein said lectin is conjugated to ferritin. --
- 804. (NEW) The process according to claim 794, wherein Sig comprises an enzyme. --

- 805. (NEW) The process according to claim 804, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, β galactosidase, ribonuclease, glucose oxidase, peroxidase, and a combination thereof. --
- 806. (NEW) The process according to claim 794, wherein Sig comprises a hormone. --
- 807. (NEW) The process according to claim 794, wherein Sig comprises a metal-containing component. --
- 808. (NEW) The process according to claim 807, wherein said metal-containing component is catalytic. --
- 809. (NEW) The process according to claim 752, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule. --
- 810. (NEW) The process according to claim 809, wherein said indicator molecule comprises an aromatic compound. --
- 811. (NEW) The process according to claim 810, wherein said aromatic compound is heterocyclic. --
- 812. (NEW) The process according to claim 811, wherein said heterocyclic aromatic compound is fluorescent. --
- 813. (NEW) The process according to claim 812, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing. --
- 814. (NEW) The process according to claim 813, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --
- 815. (NEW) The process according to claim 794, wherein Sig comprises a fluorescent component. --

- 816. (NEW) The process according to claim 815, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --
- 817. (NEW) The process according to claim 816, wherein said fluorescent component comprises fluorescein. --
- 818. (NEW) The process according to claim 794, wherein Sig comprises a chemiluminescent component. --
- 819. (NEW) The process according to claim 794, wherein Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component. --
- 820. (NEW) The process according to claim 794, wherein Sig comprises an antibody component. --
- 821. (NEW) The process according to claim 794, wherein Sig comprises a chelating component. --
- 822. (NEW) The process according to claim 809, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing. --
- 823. (NEW) The process according to claim 753, wherein A comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --
- 824. (NEW) The process according to claim 753, wherein A comprises an aliphatic chemical moiety comprising at least four carbon atoms. --
- 825. (NEW) The process according to claim 753, wherein A comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms. --

- 826. (NEW) The process according to claim 825, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent. --
- 827. (NEW) The process according to claim 753, wherein A comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --
- 828. (NEW) The process according to claim 827, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent. --
- 829. (NEW) The process according to claim 753, wherein A comprises a monosaccharide, polysaccharide or an oligosaccharide. --
- 830. (NEW) The process according to claim 753, wherein A comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --
- 831. (NEW) The process according to claim 830, wherein A comprises an electron dense component. --
- 832. (NEW) The process according to claim 831, wherein said electron dense component comprises ferritin. --
- 833. (NEW) The process according to claim 830, wherein A comprises a magnetic component. --
- 834. (NEW) The process according to claim 833, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --
- 835. (NEW) The process according to claim 833, wherein said magnetic component comprises magnetic beads. --
- 836. (NEW) The process according to claim 753, wherein A comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein. --

- 837. (NEW) The process according to claim 836, wherein the binding protein comprises a lectin. --
- 838. (NEW) The process according to claim 837, wherein the lectin comprises concanavalin A. --
- 839. (NEW) The process according to claim 837, wherein said lectin is conjugated to ferritin. --
- 840. (NEW) The process according to claim 830, wherein A comprises an enzyme. --
- 841. (NEW) The process according to claim 840, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, β -galactosidase, ribonuclease, glucose oxidase, peroxidase, and a combination thereof. --
- 842. (NEW) The process according to claim 830, wherein A comprises a hormone. --
- 843. (NEW) The process according to claim 830, wherein A comprises a metal-containing component. --
- 844. (NEW) The process according to claim 843, wherein said metal-containing component is catalytic. --
- 845. (NEW) The process according to claim 753, wherein said A comprises an indicator molecule. --
- 846. (NEW) The process according to claim 845, wherein said indicator molecule comprises an aromatic compound. --
- 847. (NEW) The process according to claim 846, wherein said aromatic compound is heterocyclic. --

- 848. (NEW) The process according to claim 847, wherein said heterocyclic aromatic compound is fluorescent. --
- 849. (NEW) The process according to claim 848, wherein said fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing. --
- 850. (NEW) The process according to claims 848 or 849, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --
- 851. (NEW) The process according to claim 830, wherein A comprises a fluorescent component. --
- 852. (NEW) The process according to claim 851, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --
- 853. (NEW) The process according to claim 852, wherein said fluorescent component comprises fluorescein. --
- 854. (NEW) The process according to claim 830, wherein A comprises a chemiluminescent component. --
- 855. (NEW) The process according to claim 830, wherein A comprises an antigenic or hapten component capable of complexing with an antibody specific to the component. --
- 856. (NEW) The process according to claim 830, wherein A comprises an antibody component. --
- 857. (NEW) The process according to claim 830, wherein A comprises a chelating component. --

-- 858. (NEW) The process according to claim 845, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing. --

859. (Amended) The process according to claim 721, wherein said detectable labeled nucleic acid fragments are detectable by a non-radioactive means selected from the group consisting of a fluorescent measurement, a chemiluminescent measurement, and a combination thereof.

-- 860. (NEW) The process according to claim 721, wherein said separating or resolving step is carried out electrophoretically. --

-- 861. (NEW) The process according to claims 721, 752 or 753, wherein said detecting step is carried out directly. --

-- 862. (NEW) The process according to claim 861, wherein said direct detection is carried out using one or more indicator molecules. --

-- 863. (NEW) The process according to claim 862, wherein said one or more indicator molecules comprise fluoresceinated nucleotides or nucleotide analogs. --

-- 864. (NEW) The process according to claim 863, wherein said fluoresceinated nucleotides or nucleotide analogs comprise fluoresceinated DNA. --

-- 865. (NEW) The process according to claim 861, wherein said detecting step is carried out by means of a directly detectable signal provided by said one or more modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety. --

--866. (NEW) The process according to claim 865, wherein in said detecting step the directly detectable signal comprises a member selected from the group consisting of a chelating compound, a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound and an electron dense compound. --

-- 867. (NEW) The process according to claim 865, wherein in said detecting step the directly detectable signal providing Sig detectable non-radioactive moiety comprises an enzyme. --

-- 868. (NEW) The process according to claims 721, 752 or 753, wherein said detecting step is carried out by means of an indirectly detectable signal provided by said one or more modified or labeled nucleotides or nucleotide analogs, said A or, said Sig detectable non-radioactive moiety. --

-- 869. (NEW) The process according to claim 868, wherein in said detecting step the indirectly detectable signal is selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme. --

~~DELETED PER 2ND SUPPL. AMEND. 8/31/00 -- 870. (NEW) The process according to claim 868, wherein in said detecting step the indirectly detectable signal is provided by a polynucleotide sequence capable of recognizing a signal containing moiety.~~

871. (Wholly Rewritten) The process according to claim 721, wherein said one or more modified or labeled nucleotides or nucleotide analogs are capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a phosphorescent measurement, a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

872. (Amended) The process according to claim 721, wherein said detecting step comprises localizing said detectable labeled nucleic acid fragments by means of said one or more modified or labeled nucleotides or nucleotide analogs.

873. (Amended) A process for determining the sequence of a nucleic acid of interest, comprising the steps of:

providing or generating detectable labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said one or more modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety or the base analog thereof;

detecting non-radioactively the detectable labeled nucleic acid fragments with a sequencing gel; and
determining the sequence of said nucleic acid of interest.

-- 874. (NEW) The process according to claim 873, wherein the nucleic acid sequence of interest is derived from an organism. --

-- 875. (NEW) The process according to claim 874, wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing. --

-- 876. (NEW) The process according to claim 875, wherein said organism comprises a mammal. --

-- 877. (NEW) The process according to claim 876, wherein said mammal comprises a human being. --

-- 878. (NEW) The process according to claim 874, wherein said organism is living. --

-- 879. (NEW) The process according to claims 874 or 878, wherein said organism is selected from the group consisting of prokaryotes and eukaryotes. --

-- 880. (NEW) The process according to claim 879, wherein said organism comprises a eukaryote. --

- 881. (NEW) The process according to claim 880, wherein said eukaryotic nucleic acid sequence of interest is contained within a chromosome. --
- 882. (NEW) The process according to claim 880, wherein said eukaryote comprises a mammal. --
- 883. (NEW) The process according to claim 882, wherein said mammalian nucleic acid sequence of interest is contained within a chromosome. --
- 884. (NEW) The process according to claim 882, wherein said mammal comprises a human being. --
- 885. (NEW) The process according to claim 884, wherein said human nucleic acid sequence of interest is contained within a chromosome. --
- 886. (NEW) The process according to claim 885, wherein said human chromosomal nucleic acid sequence of interest is part of a human gene library. --
- 887. (NEW) The process according to claim 873, wherein said providing or generating step is carried out by means of one or more primers or nucleoside triphosphates or analogs thereof. --
- 888. (NEW) The process according to claim 887, wherein said nucleoside triphosphates are selected from the group consisting of ribonucleoside triphosphates, deoxyribonucleoside triphosphates, dideoxyribonucleoside triphosphates, and analogs of any of the foregoing. --
- 889. (NEW) The process according to claim 873, wherein said fragments have been obtained or generated by a nucleic acid sequencing step or technique. --
- 890. (Amended) The process according to claim 873, wherein the detectable labeled complementary nucleic acid is fragmented and separated prior to detecting in said sequencing gel.

- 891. (NEW) The process according to claim 873, wherein in said providing or generating step, the one or more modified or labeled nucleotides or nucleotide analogs have been incorporated into said nucleic acid fragment or fragments. --
- 892. (NEW) The process according to claim 891, wherein at least one of said modified or labeled nucleotides or nucleotide analogs is at a terminus of said fragment or fragments. --
- 893. (NEW) The process according to claim 892, wherein said terminus comprises the 5' or the 3' terminus. --
- 894. (NEW) The process according to claim 891, wherein said incorporation has been carried out in the presence of a primer. --
- 895. (NEW) The process according to claim 873, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme. --
- 896. (NEW) The process according to claim 895, wherein said enzyme comprises terminal transferase. --
- 897. (NEW) The process according to claim 873, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling. --
- 898. (Wholly Rewritten) The process according to claim 897, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.
- 899. (NEW) The process according to claim 898, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase. --
- 900. (NEW) The process according to claim 873, wherein said incorporation comprises nick translation. --

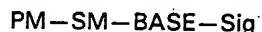
-- 901. (NEW) The process according to claim 873 or 900, wherein said incorporation is carried out by means of a polymerizing enzyme. --

--902. (NEW) The process according to claim 901, wherein said polymerizing enzyme comprises a polymerase. --

-- 903. (NEW) The process according to claim 902, wherein said polymerizing enzyme is selected from the group consisting of DNA polymerase and RNA polymerase. --

-- 904. (NEW) The process according to claim 873, wherein in said providing or generating step, the modified or labeled nucleotides or nucleotide analogs comprise one or more members selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety
or a base analog of any of the foregoing; and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

- (ii) a nucleotide or nucleotide analog having the formula

Sig

|



wherein

PM is a phosphate moiety or phosphate analog,

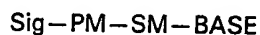
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
 Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog, said nucleotide having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

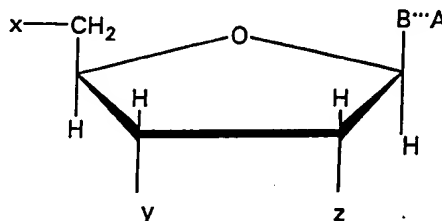
BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
 Sig is covalently attached to PM directly or through a linkage group. --

-- 905. (NEW) The process according to claim 873, wherein in said providing or
 generating step, the modified or labeled nucleotides or nucleotide analogs have the
 structure:

(i)



wherein B represents a purine moiety, a 7-deazapurine moiety, a pyrimidine
 moiety or an analog of any of the foregoing, and B is covalently bonded to the C1'-
 position of the sugar moiety or sugar analog, provided that whenever B is a purine,
 a purine analog, a 7-deazapurine moiety or a 7-deazapurine analog, the sugar
 moiety or sugar analog is attached at the N9 position of the purine moiety, the
 purine analog, the 7-deazapurine moiety or the 7-deazapurine analog thereof, and
 whenever B is a pyrimidine moiety or a pyrimidine analog, the sugar moiety or

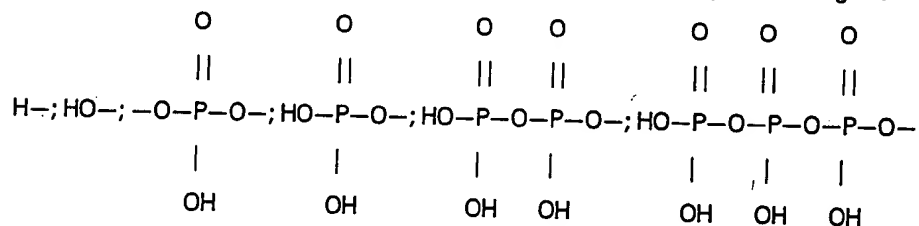
sugar analog is attached at the N1 position of the pyrimidine moiety or the pyrimidine analog;

wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal; and

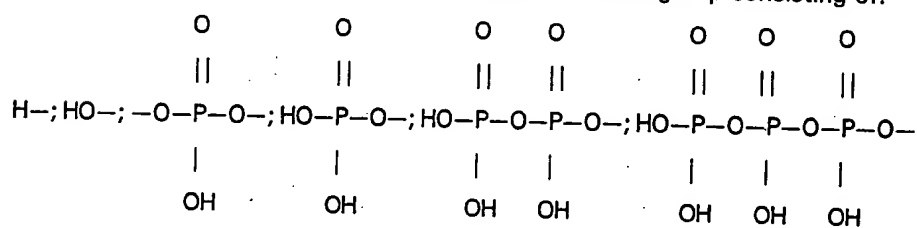
wherein B and A are covalently attached directly or through a linkage group,

wherein if B is a purine or a purine analog, A is attached to the 8-position of the purine or purine analog, if B is a 7-deazapurine or 7-deazapurine analog, A is attached to the 7-position of the deazapurine or deazapurine analog, and if B is a pyrimidine or a pyrimidine analog, A is attached to the 5-position of the pyrimidine or pyrimidine analog; and

wherein x comprises a member selected from the group consisting of:



wherein y comprises a member selected from the group consisting of:



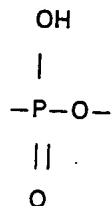
wherein z comprises a member selected from the group consisting of H- and HO-, --

-- 906. (NEW) The process according to claim 905, wherein y and z comprise H, --

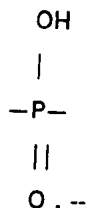
- 907. (NEW) The process according to claim 873, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a mono-phosphate, a di-phosphate, a tri-phosphate and a tetra-phosphate. --
- 908. (NEW) The process according to claim 904, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise a nucleoside mono-, di- or tri-phosphate. --
- 909. (NEW) The process according to claims 873 or 904, wherein said sugar moiety or sugar analog comprises a monosaccharide. --
- 910. (NEW) The process according to claim 909, wherein said monosaccharide comprises a furanose. --
- 911. (NEW) The process according to claim 910, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose. --
- 912. (NEW) The process according to claim 904, wherein said base moiety or base analog BASE in any of said nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --
- 913. (NEW) The process according to claim 904, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --

- 914. (NEW) The process according to claim 904, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to BASE at a position when BASE is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof. --
- 915. (NEW) The process according to claim 904, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position selected from the group consisting of the N⁴ position when said pyrimidine comprises cytosine, the N² position when said purine comprises adenine or deazaadenine, the N⁶ position when said purine comprises guanine or deazaguanine, and combinations thereof. --
- 916. (NEW) The process according to claim 910, wherein in said nucleotide (ii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --
- 917. (NEW) The process according to claim 910, wherein in said nucleotide (iii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 918. (NEW) The process according to claim 904, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of

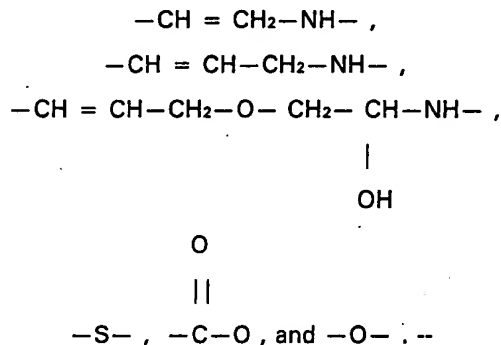


and



- 919. (NEW) The process according to claim 904, wherein PM is a mono-, di- or tri-phosphate, and wherein in said nucleotide or nucleotide analog (iii), the Sig moiety is covalently attached to PM through a phosphorus or phosphate oxygen. --
- 920. (NEW) The process according to claim 904, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal. --
- 921. (NEW) The process according to claim 904, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $\text{--CH}_2\text{NH--}$ moiety, or both. --
- 922. (NEW) The process according to claim 904, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group. --

-- 923. (NEW) The process according to claim 904, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



-- 924. (NEW) The process according to claim 904, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety. --

-- 925. (NEW) The process according to claim 904, wherein in any of said nucleotides or nucleotide analogs (i), (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group. --

-- 926. (NEW) The process according to claim 925, wherein said linkage group contains an amine. --

--927. (NEW) The process according to claim 926, wherein said amine comprises a primary amine. --

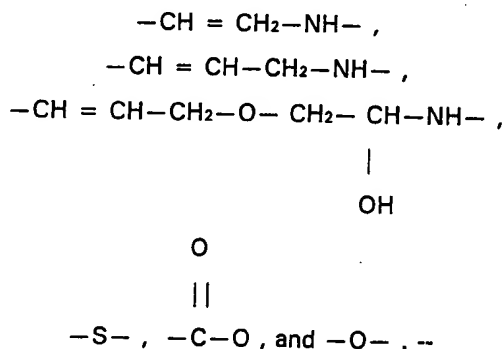
-- 928. (NEW) The process according to claim 925, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable signal. --

-- 929. (NEW) The process according to claim 905, wherein said covalent attachment does not interfere substantially with the characteristic ability of A to form a detectable non-radioactive signal. --

-- 930. (NEW) The process according to claim 905, wherein said covalent attachment comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $-\text{CH}_2\text{NH}-$ moiety, or both. --

-- 931. (NEW) The process according to claim 905, wherein said covalent attachment comprises an allylamine group. --

-- 932. (NEW) The process according to claim 905, wherein said covalent attachment comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



-- 933. (NEW) The process according to claim 905, wherein said covalent attachment includes a glycosidic linkage moiety. --

-- 934. (NEW) The process according to claim 905, wherein said A is covalently attached to B through a linkage group. --

-- 935. (NEW) The process according to claim 934, wherein said linkage group contains an amine. --

-- 936. (NEW) The process according to claim 935, wherein said amine comprises a primary amine. --

-- 937. (NEW) The process according to claim 934, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal. --

-- 938. (NEW) The process according to claim 904, wherein Sig comprises at least three carbon atoms. --

-- 939. (NEW) The process according to claim 904, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --

-- 940. (NEW) The process according to claim 904, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms. --

-- 941. (NEW) The process according to claim 904, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic moiety comprising at least five carbon atoms. --

-- 942. (NEW) The process according to claim 941, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent. --

-- 943. (NEW) The process according to claim 904, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --

-- 944. (NEW) The process according to claim 943, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent. --

-- 945. (NEW) The process according to claim 904, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide. --

-- 946. (NEW) The process according to claim 904, wherein Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --

- 947. (NEW) The process according to claim 946, wherein Sig comprises an electron dense component. --
- 948. (NEW) The process according to claim 947, wherein said electron dense component comprises ferritin. --
- 949. (NEW) The process according to claim 946, wherein Sig comprises a magnetic component. --
- 950. (NEW) The process according to claim 949, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --
- 951. (NEW) The process according to claim 949, wherein said magnetic component comprises magnetic beads. --
- 952. (NEW) The process according to claim 904, wherein Sig comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein. --
- 953. (NEW) The process according to claim 952, wherein the binding protein comprises a lectin. --
- 954. (NEW) The process according to claim 953, wherein the lectin comprises concanavalin A. --
- 955. (NEW) The process according to claim 953, wherein said lectin is conjugated to ferritin. --
- 956. (NEW) The process according to claim 946, wherein Sig comprises an enzyme. --
- 957. (NEW) The process according to claim 956, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, β -galactosidase, ribonuclease, glucose oxidase, peroxidase, and a combination thereof. --

- 958. (NEW) The process according to claim 946, wherein Sig comprises a hormone. --
- 959. (NEW) The process according to claim 946, wherein Sig comprises a metal-containing component. --
- 960. (NEW) The process according to claim 959, wherein said metal-containing component is catalytic. --
- 961. (NEW) The process according to claim 904, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule. --
- 962. (NEW) The process according to claim 961, wherein said indicator molecule comprises an aromatic compound. --
- 963. (NEW) The process according to claim 962, wherein said aromatic compound is heterocyclic. --
- 964. (NEW) The process according to claim 963, wherein said heterocyclic aromatic compound is fluorescent. --
- 965. (NEW) The process according to claim 904, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing. --
- 966. (NEW) The process according to claim 965, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --
- 967. (NEW) The process according to claim 946, wherein Sig comprises a fluorescent component. --
- 968. (NEW) The process according to claim 967, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --

- 969. (NEW) The process according to claim 968, wherein said fluorescent component comprises fluorescein. --
- 970. (NEW) The process according to claim 946, wherein Sig comprises a chemiluminescent component. --
- 971. (NEW) The process according to claim 946, wherein Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component. --
- 972. (NEW) The process according to claim 946, wherein Sig comprises an antibody component. --
- 973. (NEW) The process according to claim 946, wherein Sig comprises a chelating component. --
- 974. (NEW) The process according to claim 961, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing. --
- 975. (NEW) The process according to claim 905, wherein A comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --
- 976. (NEW) The process according to claim 905, wherein A comprises an aliphatic chemical moiety comprising at least four carbon atoms. --
- 977. (NEW) The process according to claim 905, wherein A comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms. --
- 978. (NEW) The process according to claim 977, wherein. --
- 979. (NEW) The process according to claim 905, wherein A comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --

- 980. (NEW) The process according to claim 979, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent. --
- 981. (NEW) The process according to claim 905, wherein A comprises a monosaccharide, polysaccharide or an oligosaccharide. --
- 982. (NEW) The process according to claim 905, wherein A comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --
- 983. (NEW) The process according to claim 982, wherein A comprises an electron dense component. --
- 984. (NEW) The process according to claim 983, wherein said electron dense component comprises ferritin. --
- 985. (NEW) The process according to claim 982, wherein A comprises a magnetic component. --
- 986. (NEW) The process according to claim 985, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --
- 987. (NEW) The process according to claim 985, wherein said magnetic component comprises magnetic beads. --
- 988. (NEW) The process according to claim 905, wherein A comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein. --
- 989. (NEW) The process according to claim 988, wherein the binding protein comprises a lectin. --
- 990. (NEW) The process according to claim 989, wherein the lectin comprises concanavalin A. --

- 991. (NEW) The process according to claim 989, wherein said lectin is conjugated to ferritin. --
- 992. (NEW) The process according to claim 982, wherein A comprises an enzyme. --
- 993. (NEW) The process according to claim 992, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, β -galactosidase, ribonuclease, glucose oxidase, peroxidase, and a combination thereof. --
- 994. (NEW) The process according to claim 982, wherein A comprises a hormone. --
- 995. (NEW) The process according to claim 982, wherein A comprises a metal-containing component. --
- 996. (NEW) The process according to claim 995, wherein said metal-containing component is catalytic. --
- 997. (NEW) The process according to claim 905, wherein said A comprises an indicator molecule. --
- 998. (NEW) The process according to claim 997, wherein said indicator molecule comprises an aromatic compound. --
- 999. (NEW) The process according to claim 998, wherein said aromatic compound is heterocyclic. --
- 1000. (NEW) The process according to claim 999, wherein said heterocyclic aromatic compound is fluorescent. --
- 1001. (NEW) The process according to claim 1000, wherein said fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing. --

- 1002. (NEW) The process according to claims 1000 or 1001, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --
- 1003. (NEW) The process according to claim 982, wherein A comprises a fluorescent component. --
- 1004. (NEW) The process according to claim 1003, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --
- 1005. (NEW) The process according to claim 1004, wherein said fluorescent component comprises fluorescein. --
- 1006. (NEW) The process according to claim 982, wherein A comprises a chemiluminescent component. --
- 1007. (NEW) The process according to claim 982, wherein A comprises an antigenic or hapten component capable of completing with an antibody specific to the component. --
- 1008. (NEW) The process according to claim 982, wherein A comprises an antibody component. --
- 1009. (NEW) The process according to claim 982, wherein A comprises a chelating component. --
- 1010. (NEW) The process according to claim 1009, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing. --
- 1011. (Amended) The process according to claim 873, wherein said detectable labeled nucleic acid fragments are detectable by a non-radioactive means selected from the group consisting of a fluorescent measurement, a chemiluminescent measurement, and a combination thereof.

1012. (Amended) The process according to claim 873, wherein said detecting step, the detectable labeled nucleic acid fragments are separated or resolved electrophoretically.
- 1013. (NEW) The process according to claims 873, 904 or 905, wherein said detecting step is carried out directly. --
- 1014. (NEW) The process according to claim 1013, wherein said direct detection is carried out using one or more indicator molecules. --
- 1015. (NEW) The process according to claim 1014, wherein said one or more indicator molecules comprise fluoresceinated nucleotides or nucleotide analogs. --
- 1016. (NEW) The process according to claim 1015, wherein said fluoresceinated nucleotides or nucleotide analogs comprise fluoresceinated DNA. --
- 1017. (NEW) The process according to claim 1016, wherein said detecting step is carried out by means of a directly detectable signal provided by said one or more modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety. --
- 1018. (NEW) The process according to claim 1013, wherein said detecting step the directly detectable signal comprises a member selected from the group consisting of a chelating compound, a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound and an electron dense compound. --
- 1019. (NEW) The process according to claim 1013, wherein said detecting step the directly detectable signal providing Sig detectable non-radioactive moiety comprises an enzyme. --
- 1020. (NEW) The process according to claims 873, 904 or 905, wherein said detecting step is carried out by means of an indirectly detectable signal provided by said one or more modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety. --

-- 1021. (NEW) The process according to claim 1020, wherein said detecting step the indirectly detectable signal is selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme. --

~~DELETED PER 2ND SUPPL. AMEND. 8/31/00 -- 1022. (NEW) The process according to claim 1020, wherein said detecting step the indirectly detectable signal is provided by a polynucleotide sequence capable of recognizing a signal containing moiety. --~~

1023. (Wholly Rewritten) The process according to claim 873, wherein said one or more modified or labeled nucleotides or nucleotide analogs are capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a phosphorescent measurement, a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

1024. (Amended) The process according to claim 873, wherein said detecting step comprises localizing said detectable labeled nucleic acid fragments by means of said one or more modified or labeled nucleotides or nucleotide analogs.

1025. (Amended) A process for determining the sequence of a nucleic acid of interest, comprising the step of detecting non-radioactively with a sequencing gel one or more detectable labeled nucleic acid fragments comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said one or more modified or labeled nucleotides or nucleotide analogs have been modified on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the base moiety or the base analog thereof.

-- 1026. (NEW) The process according to claim 1025, wherein the nucleic acid sequence of interest is derived from an organism. --

- 1027. (NEW) The process according to claim 1026, wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing. --
- 1028. (NEW) The process according to claim 1027, wherein said organism comprises a mammal. --
- 1029. (NEW) The process according to claim 1028, wherein said mammal comprises a human being. --
- 1030. (NEW) The process according to claim 1026, wherein said organism is living. --
- 1031. (NEW) The process according to claims 1026 or 1030, wherein said organism is selected from the group consisting of prokaryotes and eukaryotes. --
- 1032. (NEW) The process according to claim 1031, wherein said organism comprises a eukaryote. --
- 1033. (NEW) The process according to claim 1032, wherein said eukaryotic nucleic acid sequence of interest is contained within a chromosome. --
- 1034. (NEW) The process according to claim 1032, wherein said eukaryote comprises a mammal. --
- 1035. (NEW) The process according to claim 1034, wherein said mammalian nucleic acid sequence of interest is contained within a chromosome. --
- 1036. (NEW) The process according to claim 1034, wherein said mammal comprises a human being. --
- 1037. (NEW) The process according to claim 1036, wherein said human nucleic acid sequence of interest is contained within a chromosome. --
- 1038. (NEW) The process according to claim 1037, wherein said human chromosomal nucleic acid sequence of interest is part of a human gene library. --

-- 1039. (NEW) The process according to claim 1025, wherein said providing or generating step is carried out by means of one or more primers or nucleoside triphosphates or analogs thereof. --

-- 1040. (NEW) The process according to claim 1039, wherein said nucleoside triphosphates are selected from the group consisting of ribonucleoside triphosphates, deoxyribonucleoside triphosphates, dideoxyribonucleoside triphosphates, and analogs of any of the foregoing. --

-- 1041. (NEW) The process according to claim 1025, wherein said fragments have been obtained or generated by a nucleic acid sequencing step or technique. --

1042. (Amended) The process according to claim 1025, wherein the detectable labeled complementary nucleic acid is fragmented prior to separation in said sequencing gel.

-- 1043. (NEW) The process according to claim 1025, wherein said providing or generating step, the one or more modified or labeled nucleotides or nucleotide analogs have been incorporated into said nucleic acid fragment or fragments. --

-- 1044. (NEW) The process according to claim 1043, wherein at least one of said modified or labeled nucleotides or nucleotide analogs is at a terminus of said fragment or fragments. --

-- 1045. (NEW) The process according to claim 1044, wherein said terminus comprises the 5' or the 3' terminus. --

-- 1046. (NEW) The process according to claim 1043, wherein said incorporation has been carried out in the presence of a primer. --

-- 1047. (NEW) The process according to claim 1025, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme. --

-- 1048. (NEW) The process according to claim 1047, wherein said enzyme comprises terminal transferase. --

-- 1049. (NEW) The process according to claim 1025, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling. --

1050. (Wholly Rewritten) The process according to claim 1049, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.

-- 1051. (NEW) The process according to claim 1049, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase. --

-- 1052. (NEW) The process according to claim 1025, wherein said incorporation comprises nick translation. --

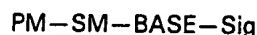
-- 1053. (NEW) The process according to claim 1025 or 1052, wherein said incorporation is carried out by means of a polymerizing enzyme. --

-- 1054. (NEW) The process according to claim 1053, wherein said polymerizing enzyme comprises a polymerase. --

-- 1055. (NEW) The process according to claim 1054, wherein said polymerase is selected from the group consisting of DNA polymerase and RNA polymerase. --

-- 1056. (NEW) The process according to claim 1025, wherein said providing or generating step, the modified or labeled nucleotides or nucleotide analogs comprise one or more members selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

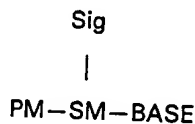
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety

or a base analog of any of the foregoing; and

Sig is a detectable non-radioactive moiety,
wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
Sig is covalently attached to BASE directly or through a linkage group at a position
other than the C5 position when BASE is a pyrimidine moiety or an analog thereof,
at a position other than the C8 position when BASE is a purine moiety or an analog
thereof and at a position other than the C7 position when BASE is a 7-deazapurine
moiety or an analog thereof;

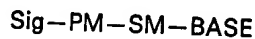
(ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,
SM is a sugar moiety or sugar analog,
BASE is a base moiety or base analog, and
Sig is a detectable non-radioactive moiety,
wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog, said nucleotide having the formula

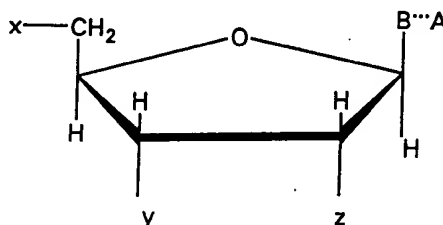


wherein

PM is a phosphate moiety or phosphate analog,
SM is a sugar moiety or sugar analog,
BASE is a base moiety or base analog, and
Sig is a detectable non-radioactive moiety,
wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
Sig is covalently attached to PM directly or through a linkage group. --

-1057. (NEW) The process according to claim 1025, wherein said providing or generating step, the modified or labeled nucleotides or nucleotide analogs have the structure:

(i)



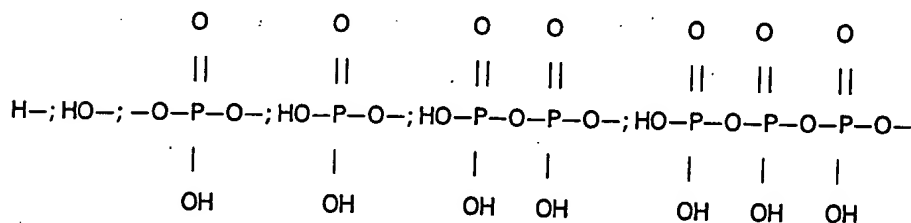
wherein B represents a purine moiety, a 7-deazapurine moiety, a pyrimidine moiety, or an analog of any of the foregoing, and B is covalently bonded to the C1'-position of the sugar moiety or sugar analog, provided that whenever B is a purine, a purine analog, a 7-deazapurine moiety or a 7-deazapurine analog, the sugar moiety or sugar analog is attached at the N9 position of the purine moiety, the purine analog, the 7-deazapurine moiety or the 7-deazapurine analog thereof, and whenever B is a pyrimidine moiety or a pyrimidine analog, the sugar moiety or sugar analog is attached at the N1 position of the pyrimidine moiety or the pyrimidine analog;

wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal; and

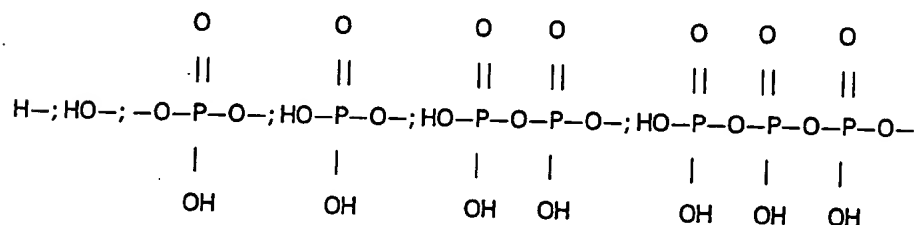
wherein B and A are covalently attached directly or through a linkage group,

wherein if B is a purine or a purine analog, A is attached to the 8-position of the purine or purine analog, if B is a 7-deazapurine or 7-deazapurine analog, A is attached to the 7-position of the deazapurine or deazapurine analog, and if B is a pyrimidine or a pyrimidine analog, A is attached to the 5-position of the pyrimidine or pyrimidine analog; and

wherein x comprises a member selected from the group consisting of:



wherein y comprises a member selected from the group consisting of:



wherein z comprises a member selected from the group consisting of H- and HO-. --

--1058. (NEW) The process according to claim 1057, wherein y and z comprise H. --

-- 1059. (NEW) The process according to claim 1025, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a mono-phosphate, a di-phosphate, a tri-phosphate and a tetra-phosphate. --

-- 1060. (NEW) The process according to claim 1056, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise a nucleoside mono-, di- or tri-phosphate. --

-- 1061. (NEW) The process according to claims 1025 or 1056, wherein said sugar moiety or sugar analog comprises a monosaccharide. --

-- 1062. (NEW) The process according to claim 1061, wherein said monosaccharide comprises a furanose. --

-- 1063. (NEW) The process according to claim 1062, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose. --

-- 1064. (NEW) The process according to claim 1056, wherein said base moiety or base analog BASE in any of said nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --

-- 1065. (NEW) The process according to claim 1056, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --

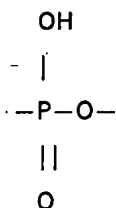
-- 1066. (NEW) The process according to claim 1056, wherein said Sig detectable non-radioactive moiety in said nucleotide M is covalently attached to said BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to BASE at a position when BASE is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof. --

-- 1067. (NEW) The process according to claim 1056, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position selected from the group consisting of the N⁴ position when said pyrimidine comprises cytosine, the N² position when said purine comprises adenine or deazaadenine, the N⁶ position when said purine comprises guanine or deazaguanine, and combinations thereof. --

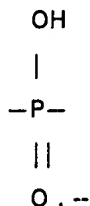
-- 1068. (NEW) The process according to claim 1062, wherein in said nucleotide (ii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 1069. (NEW) The process according to claim 1062, wherein in said nucleotide (iii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 1070. (NEW) The process according to claim 1056, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



and



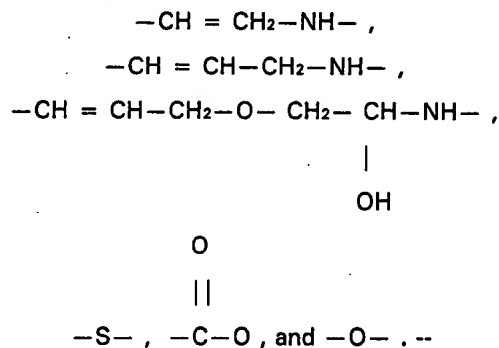
-- 1071. (NEW) The process according to claim 1056, wherein PM is a mono-, di or tri-phosphate, and wherein said nucleotide or nucleotide analog (iii), the Sig moiety is covalently attached to PM through a phosphorus or phosphate oxygen. --

-- 1072. (NEW) The process according to claim 1056, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal. --

-- 1073. (NEW) The process according to claim 1056, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $-\text{CH}_2\text{NH}-$ moiety, or both. --

-- 1074. (NEW) The process according to claim 1056, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group. --

-- 1075. (NEW) The process according to claim 1056, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



--1076. (NEW) The process according to claim 1056, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety. --

-- 1077. (NEW) The process according to claim 1056, wherein in any of said nucleotides or nucleotide analogs (i), (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group. --

-- 1078. (NEW) The process according to claim 1077, wherein said linkage group contains an amine. --

-- 1079. (NEW) The process according to claim 1078, wherein said amine comprises a primary amine. --

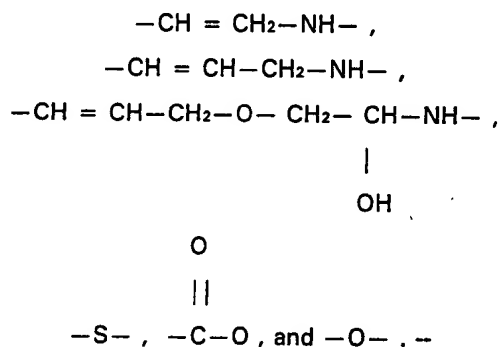
-- 1080. (NEW) The process according to claim 1077, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal. --

-- 1081. (NEW) The process according to claim 1057, wherein said covalent attachment does not interfere substantially with the characteristic ability of A to form a detectable non-radioactive signal. --

-- 1082. (NEW) The process according to claim 1057, wherein said covalent attachment comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $-\text{CH}_2\text{NH}-$ moiety, or both. --

-- 1083. (NEW) The process according to claim 1057, wherein said covalent attachment comprises an allylamine group. --

-- 1084. (NEW) The process according to claim 1057, wherein said covalent attachment comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



-- 1085. (NEW) The process according to claim 1057, wherein said covalent attachment includes a glycosidic linkage moiety. --

-- 1086. (NEW) The process according to claim 1057, wherein said A is covalently attached to B through a linkage group. --

- 1087. (NEW) The process according to claim 1086, wherein said linkage group contains an amine. --
- 1088. (NEW) The process according to claim 1087, wherein said amine comprises a primary amine. --
- 1089. (NEW) The process according to claim 1086, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal. --
- 1090. (NEW) The process according to claim 1056, wherein Sig comprises at least three carbon atoms. --
- 1091. (NEW) The process according to claim 1056, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --
- 1092. (NEW) The process according to claim 1056, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms. --
- 1093. (NEW) The process according to claim 1056, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic moiety comprising at least five carbon atoms. --
- 1094. (NEW) The process according to claim 1093, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent. --
- 1095. (NEW) The process according to claim 1056, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --
- 1096. (NEW) The process according to claim 1095, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent. --

- 1097. (NEW) The process according to claim 1056, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide. --
- 1098. (NEW) The process according to claim 1056, wherein Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --
- 1099. (NEW) The process according to claim 1098, wherein Sig comprises an electron dense component. --
- 1100. (NEW) The process according to claim 1099, wherein said electron dense component comprises ferritin. --
- 1101. (NEW) The process according to claim 1098, wherein Sig comprises a magnetic component. --
- 1102. (NEW) The process according to claim 1101, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --
- 1103. (NEW) The process according to claim 1101, wherein said magnetic component comprises magnetic beads. --
- 1104. (NEW) The process according to claim 1056, wherein Sig comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein. --
- 1105. (NEW) The process according to claim 1104, wherein the binding protein comprises a lectin. --
- 1106. (NEW) The process according to claim 1105, wherein the lectin comprises concanavalin A. --
- 1107. (NEW) The process according to claim 1105, wherein said lectin is conjugated to ferritin. --

-- 1108. (NEW) The process according to claim 1098, wherein Sig comprises an enzyme. --

-- 1109. (NEW) The process according to claim 1108, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, β -galactosidase, ribonuclease, glucose oxidase, peroxidase, and a combination thereof. --

-- 1110. (NEW) The process according to claim 1098, wherein Sig comprises a hormone. --

-- 1111. (NEW) The process according to claim 1098, wherein Sig comprises a metal-containing component. --

-- 1112. (NEW) The process according to claim 1111, wherein said metal-containing component is catalytic. --

--1113. (NEW) The process according to claim 1056, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule. --

-- 1114. (NEW) The process according to claim 1113, wherein said indicator molecule comprises an aromatic compound. --

-- 1115. (NEW) The process according to claim 1114, wherein said aromatic compound is heterocyclic. --

-- 1116. (NEW) The process according to claim 1115, wherein said heterocyclic aromatic compound is fluorescent. --

-- 1117. (NEW) The process according to claim 1116, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing. --

-- 1118. (NEW) The process according to claim 1117, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --

-- 1119. (NEW) The process according to claim 1098, wherein Sig comprises a fluorescent component. --

-- 1120. (NEW) The process according to claim 1119, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --

-- 1121. (NEW) The process according to claim 1120, wherein said fluorescent component comprises fluorescein. --

--1122. (NEW) The process according to claim 1098, wherein Sig comprises a chemiluminescent component. --

-- 1123. (NEW) The process according to claim 1098, wherein Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component. --

-- 1124. (NEW) The process according to claim 1098, wherein Sig comprises an antibody component. --

-- 1125. (NEW) The process according to claim 1098, wherein Sig comprises a chelating component. --

-- 1126. (NEW) The process according to claim 1113, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing. --

-- 1127. (NEW) The process according to claim 1057, wherein A comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --

-- 1128. (NEW) The process according to claim 1057, wherein A comprises an aliphatic chemical moiety comprising at least four carbon atoms. --

- 1129. (NEW) The process according to claim 1057, wherein A comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms. --
- 1130. (NEW) The process according to claim 1129, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent. --
- 1131. (NEW) The process according to claim 1057, wherein A comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --
- 1132. (NEW) The process according to claim 1131, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent. --
- 1133. (NEW) The process according to claim 1057, wherein A comprises a monosaccharide, polysaccharide or an oligosaccharide. --
- 1134. (NEW) The process according to claim 1057, wherein A comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --
- 1135. (NEW) The process according to claim 1134, wherein A comprises an electron dense component. --
- 1136. (NEW) The process according to claim 1135, wherein said electron dense component comprises ferritin. --
- 1137. (NEW) The process according to claim 1134, wherein A comprises a magnetic component. --
- 1138. (NEW) The process according to claim 1137, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --
- 1139. (NEW) The process according to claim 1137, wherein said magnetic component comprises magnetic beads. --

- 1140. (NEW) The process according to claim 1057, wherein A comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein. --
- 1141. (NEW) The process according to claim 1140, wherein the binding protein comprises a lectin. --
- 1142. (NEW) The process according to claim 1141, wherein the lectin comprises concanavalin A. --
- 1143. (NEW) The process according to claim 1141, wherein said lectin is conjugated to ferritin. --
- 1144. (NEW) The process according to claim 1134, wherein A comprises an enzyme. --
- 1145. (NEW) The process according to claim 1144, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, β -galactosidase, ribonuclease, glucose oxidase, peroxidase, and a combination thereof. --
- 1146. (NEW) The process according to claim 1134, wherein A comprises a hormone. --
- 1147. (NEW) The process according to claim 1134, wherein A comprises a metal-containing component. --
- 1148. (NEW) The process according to claim 1147, wherein said metal-containing component is catalytic. --
- 1149. (NEW) The process according to claim 1057, wherein said A comprises an indicator molecule. --
- 1150. (NEW) The process according to claim 1149, wherein said indicator molecule comprises an aromatic compound. --

- 1151. (NEW) The process according to claim 1150, wherein said aromatic compound is heterocyclic. --
- 1152. (NEW) The process according to claim 1151, wherein said heterocyclic aromatic compound is fluorescent. --
- 1153. (NEW) The process according to claim 1152, wherein said fluorescent, heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing. --
- 1154. (NEW) The process according to claims 1152 or 1153, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --
- 1155. (NEW) The process according to claim 1154, wherein A comprises a fluorescent component. --
- 1156. (NEW) The process according to claim 1155, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --
- 1157. (NEW) The process according to claim 1156, wherein said fluorescent component comprises fluorescein. --
- 1158. (NEW) The process according to claim 1134, wherein A comprises a chemiluminescent component. --
- 1159. (NEW) The process according to claim 1134, wherein A comprises an antigenic or hapten component capable of completing with an antibody specific to the component. --
- 1160. (NEW) The process according to claim 1134, wherein A comprises an antibody component. --
- 1161. (NEW) The process according to claim 1134, wherein A comprises a chelating component. --

-- 1162. (NEW) The process according to claim 1149, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing. --

1163. (Amended) The process according to claim 1025, wherein said detectable labeled nucleic acid fragments are detectable by a non-radioactive means selected from the group consisting of a fluorescent measurement, a chemiluminescent measurement, and a combination thereof.

1164. (Amended) The process according to claim 1025, wherein said detecting step, the detectable labeled nucleic acid fragments are separated or resolved electrophoretically.

-- 1165. (NEW) The process according to claims 1025, 1056 or 1057, wherein said detecting step is carried out directly. --

-- 1166. (NEW) The process according to claim 1165, wherein said direct detection is carried out using one or more indicator molecules. --

-- 1167. (NEW) The process according to claim 1166, wherein said one or more indicator molecules comprise fluoresceinated nucleotides or nucleotide analogs. --

-- 1168. (NEW) The process according to claim 1167, wherein said fluoresceinated nucleotides or nucleotide analogs comprise fluoresceinated DNA. --

-- 1169. (NEW) The process according to claim 1165, wherein said detecting step is carried out by means of a directly detectable signal provided by said one or more modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety. --

-- 1170. (NEW) The process according to claim 1165, wherein said detecting step the directly detectable signal comprises a member selected from the group consisting of a chelating compound, a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound and an electron dense compound. --

-- 1171. (NEW) The process according to claim 1165, wherein said detecting step the directly detectable signal comprises an enzyme. --

-- 1172. (NEW) The process according to claims 1025, 1056 or 1057, wherein said detecting step is carried out by means of an indirectly detectable signal provided by said one or more modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety. --

-- 1173. (NEW) The process according to claim 1172, wherein said detecting step the indirectly detectable signal is selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme. --

~~DELETED PER 2ND SUPPL. AMEND. 8/31/00 -- 1174. (NEW) The process according to claim 1172, wherein said detecting step the indirectly detectable signal is provided by a polynucleotide sequence capable of recognizing a signal containing moiety. --~~

1175. (Wholly Rewritten) The process according to claim 1025, wherein said one or more modified or labeled nucleotides or nucleotide analogs are capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a phosphorescent measurement, a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

1176. (Amended) The process according to claim 1025, wherein said detecting step comprises localizing said detectable labeled nucleic acid fragments by means of said one or more modified or labeled nucleotides or nucleotide analogs.

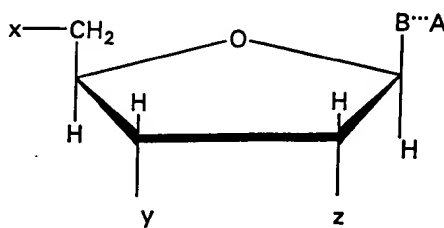
1177. (Amended) A process for determining with a sequencing gel the presence of nucleic acid fragments comprising a sequence complementary to a nucleic acid of interest or a portion thereof, said process comprising the steps of:

- (A) providing
 - (i) one or more detectable chemically modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into a nucleic acid; or
 - (ii) one or more oligonucleotides or polynucleotides comprising at least one said detectable chemically modified or labeled nucleotide or nucleotide analog; or
 - (iii) both (i) and (ii);

wherein said chemically modified or labeled nucleotides or nucleotide analogs (i) and said oligonucleotides and polynucleotides (ii) are capable of attaching to or coupling to or incorporating into or forming one or more nucleic acid fragments, and wherein said chemically modified or labeled nucleotides or nucleotide analogs have been modified or labeled non-disruptively or disruptively on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety or the base analog thereof; and;

(B) incorporating said one or more chemically modified or labeled nucleotides or nucleotide analogs (i) or said one or more oligonucleotides or polynucleotides comprising at least one chemically modified or labeled nucleotides or nucleotide analogs (ii), or both (i) and (ii), into one or more nucleic acid fragments, to prepare detectable labeled fragments, each such fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof and said one or more chemically modified or labeled nucleotides or nucleotide analogs, and wherein said chemically modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

(i)

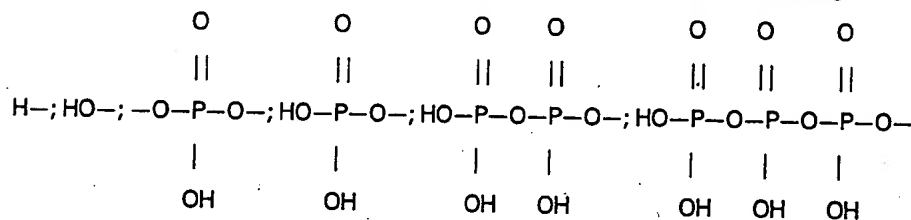


wherein B represents a purine moiety, a 7-deazapurine moiety, a pyrimidine moiety, or an analog of any of the foregoing, and B is covalently bonded to the C1-position of the sugar moiety or sugar analog, provided that whenever B is a purine, a purine analog, a 7-deazapurine moiety or a 7-deazapurine analog, the sugar moiety or sugar analog is attached at the N9 position of the purine moiety, the purine analog, the 7-deazapurine moiety or the 7-deazapurine analog thereof, and, whenever B is a pyrimidine moiety or a pyrimidine analog, the sugar moiety or sugar analog is attached at the N1 position of the pyrimidine moiety or the pyrimidine analog;

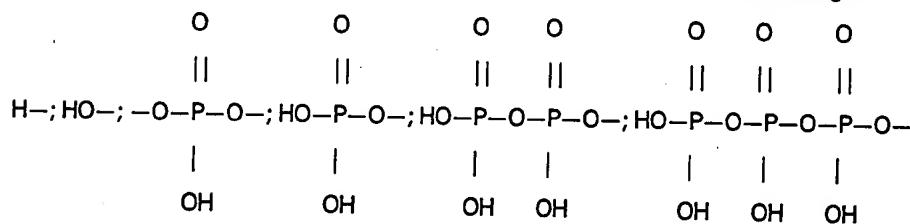
wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal; and

wherein B and A are covalently attached directly or through a linkage group, and

wherein x comprises a member selected from the group consisting of:



wherein y comprises a member selected from the group consisting of:



wherein z comprises a member selected from the group consisting of H- and HO-;

(ii)

Sig

|

PM—SM—BASE

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety, and

wherein said PM is covalently attached to SM, said BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii)

Sig—PM—SM—BASE

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is detectable non-radioactive moiety; and

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

(C) transferring or subjecting said detectable labeled fragments to a sequencing gel;

(D) separating or resolving said detectable labeled fragments; and

(E) non-radioactively detecting directly or indirectly the presence of said detectable labeled fragments.

-- 1178. (NEW) The process according to claim 1177, wherein the nucleic acid sequence of interest is derived from an organism. --

- 1179. (NEW) The process according to claim 1178, wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing. --
- 1180. (NEW) The process according to claim 1179, wherein said organism comprises a mammal. --
- 1181. (NEW) The process according to claim 1180, wherein said mammal comprises a human being. --
- 1182. (NEW) The process according to claim 1178, wherein said organism is living. --
- 1183. (NEW) The process according to claims 1178 or 1182, wherein said organism is selected from the group consisting of prokaryotes and eukaryotes. --
- 1184. (NEW) The process according to claim 1183, wherein said organism comprises a eukaryote. --
- 1185. (NEW) The process according to claim 1184, wherein said eukaryotic nucleic acid sequence of interest is contained within a chromosome. --
- 1186. (NEW) The process according to claim 1184, wherein said eukaryote comprises a mammal. --
- 1187. (NEW) The process according to claim 1186, wherein said mammalian nucleic acid sequence of interest is contained within a chromosome. --
- 1188. (NEW) The process according to claim 1186, wherein said mammal comprises a human being. --
- 1189. (NEW) The process according to claim 1188, wherein said human nucleic acid sequence of interest is contained within a chromosome. --

- 1190. (NEW) The process according to claim 1189, wherein said human chromosomal nucleic acid sequence of interest is part of a human gene library. --
- 1191. (NEW) The process according to claim 1177, wherein said incorporating step is carried out using an enzyme. --
- 1192. (NEW) The process according to claim 1191, wherein said enzyme comprises a polymerase. --
- 1193. (NEW) The process according to claim 1192, wherein said polymerase comprises DNA polymerase. --
- 1194. (NEW) The process according to claim 1177, wherein said one or more chemically modified nucleotides or said other modified or unmodified nucleic acids comprise a nucleoside di- or tri-phosphate. --
- 1195. (NEW) The process according to claim 1177, wherein said incorporating step is template dependent or template independent. --
- 1196. (NEW) The process according to claim 1177, wherein said incorporating step is template dependent. --
- 1197. (Amended) The process according to claim 1177, wherein the detectable labeled nucleic acid fragments prepared by said incorporating step comprises at least one internal modified nucleotide.
- 1198. (Amended) The process according to claim 1177, wherein the detectable labeled nucleic acid fragments prepared by said incorporating step comprises at least one terminal modified nucleotide.
- 1199. (NEW) The process according to claim 1177, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme. --
- 1200. (NEW) The process according to claim 1199, wherein said enzyme comprises terminal transferase. --

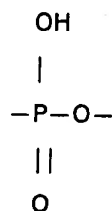
- 1201. (NEW) The process according to claim 1177, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling. --
1202. (Wholly Rewritten) The process according to claim 1201, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.
- 1203. (NEW) The process according to claim 1201, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase. --
- 1204. (NEW) The process according to claim 1177, wherein said incorporation comprises nick translation. --
- 1205. (NEW) The process according to claim 1177 or 1204, wherein said incorporation is carried out by means of a polymerizing enzyme. --
- 1206. (NEW) The process according to claim 1205, wherein said polymerizing enzyme comprises a polymerase. --
- 1207. (NEW) The process according to claim 1206, wherein said polymerase is selected from the group consisting of DNA polymerase and RNA polymerase. --
- 1208. (NEW) The process according to claim 1177, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a monophosphate, a di-phosphate, a tri-phosphate and a tetra-phosphate. --
- 1209. (NEW) The process according to claim 1177, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise a nucleoside mono-, di- or tri-phosphate. --
- 1210. (NEW) The process according to claim 1177, wherein said sugar moiety or sugar analog comprises a monosaccharide. --

- 1211. (NEW) The process according to claim 1210, wherein said monosaccharide comprises a furanose. --
- 1212. (NEW) The process according to claim 1211, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose. --
- 1213. (NEW) The process according to claim 1177, wherein said B in nucleotide or nucleotide analog (i) or said BASE in nucleotides or nucleotide analogs (ii) or (iii) is selected from the group consisting of a pyrimidine moiety or pyrimidine analog, a purine moiety or purine analog, a 7-deazapurine moiety and a 7-deazapurine analog, and a combination of any of the foregoing. --
- 1214. (NEW) The process according to claim 1177, wherein in said chemically modified nucleotides or nucleotide analogs (i) when B is a purine or a purine analog, A is attached to the 8-position of the purine moiety or the purine analog, when B is a 7-deazapurine moiety or a 7-deazapurine analog, A is attached to the 7-position of the deazapurine moiety or the 7-deazapurine analog, and when B is a pyrimidine moiety or a pyrimidine analog, A is attached to the 5-position of the pyrimidine moiety or the pyrimidine analog. --
- 1215. (NEW) The process according to claim 1177, wherein in said chemically modified nucleotides or nucleotide analogs (i) A is covalently attached to said B at a position when B is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to B at a position when B is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof. --
- 1216. (NEW) The process according to claim 1177, wherein in said chemically modified nucleotides or nucleotide analogs (i) A is covalently attached to said B at a position selected from the group consisting of the N⁴ position when said pyrimidine comprises cytosine, the N² position when said purine comprises adenine or deazaadenine, the N⁶ position when said purine comprises guanine or deazaguanine, and combinations thereof. --

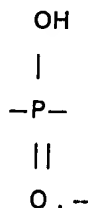
- 1217. (NEW) The process according to claim 1177, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i) or (iii) or both is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --
- 1218. (NEW) The process according to claim 1177, wherein said incorporating step, A in the nucleotide (i) is covalently attached to B through a linkage group. --
- 1219. (NEW) The process according to claim 1218, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal. --
- 1220. (NEW) The process according to claim 1218, wherein said linkage group contains an amine. --
- 1221. (NEW) The process according to claim 1220, wherein said amine comprises a primary amine. --
- 1222. (NEW) The process according to claim 1177, wherein said incorporating step, Sig in the nucleotide (ii) is covalently attached to SM through a linkage group. --
- 1223. (NEW) The process according to claim 1222, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal. --
- 1224. (NEW) The process according to claim 1222, wherein said linkage group contains an amine. --
- 1225. (NEW) The process according to claim 1224, wherein said amine comprises a primary amine. --
- 1226. (NEW) The process according to claim 1177, wherein said incorporating step, Sig in the nucleotide (iii) is covalently attached to PM through a linkage group. --

- 1227. (NEW) The process according to claim 1226, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal. --
- 1228. (NEW) The process according to claim 1226, wherein said linkage group contains an amine. --
- 1229. (NEW) The process according to claim 1228, wherein said amine comprises a primary amine. --
- 1230. (NEW) The process according to claim 1211, wherein in said nucleotide (ii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --
- 1231. (NEW) The process according to claim 1211, wherein in said nucleotide (iii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 1232. (NEW) The process according to claim 1177, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



and



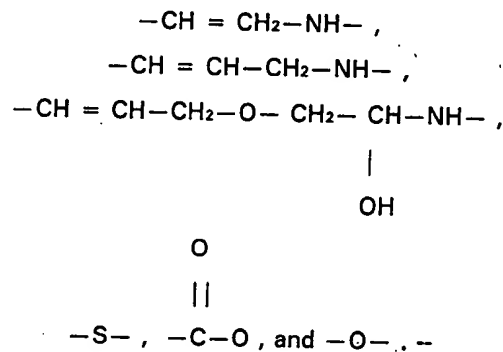
-- 1233. (NEW) The process according to claim 1177, wherein PM is a mono-, di- or tri-phosphate, and wherein in said nucleotide or nucleotide analog (iii), the Sig moiety is covalently attached to PM through a phosphorus or phosphate oxygen. --

-- 1234. (NEW) The process according to claim 1177, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of A or Sig to form a detectable non-radioactive signal. --

1235. (Amended) The process according to claim 1177, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $[-\text{CH}_2\text{NH}-]$ $-\text{CH}_2\text{NH}-$ moiety, or both.

-- 1236. (NEW) The process according to claim 1177, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group. --

-- 1237. (NEW) The process according to claim 1177, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



-- 1238. (NEW) The process according to claim 1177, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety. --

-- 1239. (NEW) The process according to claim 1177, wherein in said nucleotides or nucleotide analogs (i), A is covalently attached to B through a linkage group, or in said nucleotides or nucleotide analogs (ii) or (iii), Sig is covalently attached to BASE, SM or PM through a linkage group. --

-- 1240. (NEW) The process according to claim 1239, wherein said linkage group contains an amine. --

-- 1241. (NEW) The process according to claim 1240, wherein said amine comprises a primary amine. --

-- 1242. (NEW) The process according to claim 1239, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal. --

-- 1243. (NEW) The process according to claim 1177, wherein said A or Sig comprises at least three carbon atoms. --

- 1244. (NEW) The process according to claim 1177, wherein said A or Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --
- 1245. (NEW) The process according to claim 1177, wherein said A or Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms. --
- 1246. (NEW) The process according to claim 1177, wherein said A or Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms. --
- 1247. (NEW) The process according to claim 1141, wherein said A or Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --
- 1248. (NEW) The process according to claim 1177, wherein said A or Sig comprises a monosaccharide, polysaccharide or an oligosaccharide. --
- 1249. (NEW) The process according to claim 1177, wherein said A or Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --
- 1250. (NEW) The process according to claim 1249, wherein said A or Sig comprises an electron dense component. --
- 1251. (NEW) The process according to claim 1250, wherein said electron dense component comprises ferritin. --
- 1252. (NEW) The process according to claim 1249, wherein said A or Sig comprises a magnetic component. --

- 1253. (NEW) The process according to claim 1252, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --
- 1254. (NEW) The process according to claim 1252, wherein said magnetic component comprises magnetic beads. --
- 1255. (NEW) The process according to claim 1177, wherein said A or Sig comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein. --
- 1256. (NEW) The process according to claim 1255, wherein the binding protein comprises a lectin. --
- 1257. (NEW) The process according to claim 1256, wherein the lectin comprises concanavalin A. --
- 1258. (NEW) The process according to claim 1256, wherein said lectin is conjugated to ferritin. --
- 1259. (NEW) The process according to claim 1249, wherein said A or Sig comprises an enzyme. --
- 1260. (NEW) The process according to claim 1259, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, β -galactosidase, ribonuclease, glucose oxidase and peroxidase, or a combination thereof. --
- 1261. (NEW) The process according to claim 1249, wherein said A or Sig comprises a hormone. --
- 1262. (NEW) The process according to claim 1249, wherein said A or Sig comprises a metal-containing component. --
- 1263. (NEW) The process according to claim 1262, wherein said metal-containing component is catalytic. --

- 1264. (NEW) The process according to claim 1177, wherein said A or Sig detectable non-radioactive moiety comprises an indicator molecule. --
- 1265. (NEW) The process according to claim 1264, wherein said indicator molecule comprises an aromatic compound. --
- 1266. (NEW) The process according to claim 1265, wherein said aromatic compound is heterocyclic. --
- 1267. (NEW) The process according to claim 1266, wherein said heterocyclic aromatic compound is fluorescent. --
- 1268. (NEW) The process according to claim 1267, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine and dansyl. --
- 1269. (NEW) The process according to claim 1268, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --
- 1270. (NEW) The process according to claim 1264, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, and a chelating component, or a combination of any of the foregoing. --
- 1271. (NEW) The process according to claim 1249, wherein said A or Sig comprises a fluorescent component. --
- 1272. (NEW) The process according to claim 1271, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --
- 1273. (NEW) The process according to claim 1272, wherein said fluorescent component comprises fluorescein. --
- 1274. (NEW) The process according to claim 1249, wherein said A or Sig comprises a chemiluminescent component. --

- 1275. (NEW) The process according to claim 1249, wherein said A or Sig comprises an antigenic or hapten component capable of completing with an antibody specific to the component. --
- 1276. (NEW) The process according to claim 1249, wherein said A or Sig comprises an antibody component. --
- 1277. (NEW) The process according to claim 1249, wherein said A or Sig comprises a chelating component. --
- 1278. (NEW) The process according to claim 1177, wherein any of nucleotide or nucleotide analogs (i), (ii) and (iii) are detectable by a means selected from the group consisting of a fluorescent measurement and a chemiluminescent measurement, or a combination thereof. --
- 1279. (NEW) The process according to claim 1177, wherein said A or Sig is detectable when it is attached to the nucleotide or nucleotide analog directly or through a linkage group. --
- 1280. (NEW) The process according to claim 1279, wherein said linkage group does not interfere substantially with the characteristic ability of A or Sig to form a detectable non-radioactive signal. --
1281. (Amended) The process according to claim 1177, wherein said detectable labeled nucleic acid fragment or fragments are terminally ligated or attached to a polypeptide.
- 1282. (NEW) The process according to claim 1281, wherein the polypeptide comprises a polylysine. --
- 1283. (NEW) The process according to claim 1281, wherein the polypeptide comprises at least one member selected from the group consisting of avidin, streptavidin or anti-Sig immunoglobulin. --

- 1284. (NEW) The process according to claim 1281, wherein said A or Sig comprises a ligand and the polypeptide comprises an antibody thereto. --
- 1285. (NEW) The process according to claim 1177, wherein said separating step is carried out electrophoretically. --
- 1286. (NEW) The process according to claim 1177, wherein said detecting step is carried out directly. --
- 1287. (NEW) The process according to claim 1286, wherein said direct detection is carried out on one or more indicator molecules. --
- 1288. (NEW) The process according to claim 1287, wherein said one or more indicator molecules comprise fluoresceinated nucleotides. --
- 1289. (NEW) The process according to claim 1288, wherein said fluoresceinated nucleotides or nucleotide analogs comprise fluoresceinated DNA. --
- 1290. (NEW) The process according to claim 1177, wherein said detecting step is carried out by means of a directly detectable signal provided by said A or Sig detectable non-radioactive moiety. --
- 1291. (NEW) The process according to claim 1290, wherein said detecting step the directly detectable signal providing A or Sig detectable non-radioactive moiety comprises a member selected from the group consisting of a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound and an electron dense compound. --
- 1292. (NEW) The process according to claim 1290, wherein said detecting step the directly detectable signal is provided by an enzyme. --
- 1293. (NEW) The process according to claim 1177, wherein said detecting step is carried out by means of an indirectly detectable signal provided by said A or Sig detectable non-radioactive moiety. --

-- 1294. (NEW) The process according to claim 1293, wherein said detecting step the indirectly detectable signal is provided by a member selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme. --

~~DELETED PER 2ND SUPPL. AMEND. 8/31/00 -- 1295. (NEW) The process according to claim 1293, wherein said detecting step the indirectly detectable signal providing Sig detectable non-radioactive moiety comprises a polynucleotide sequence capable of recognizing a signal containing moiety.~~

-- 1296. (NEW) The process according to claim 1293, wherein said detecting step the indirectly detectable signal providing Sig detectable non-radioactive moiety comprises a compound capable of binding to an insoluble phase. --

1297. (Wholly Rewritten) The process according to claim 1177, wherein said Sig detectable non-radioactive moiety is capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a phosphorescent measurement, a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

1298. (Amended) A process for detecting a nucleic acid of interest in a sample, which process comprises the steps of:

(a) specifically hybridizing said nucleic acid of interest in the sample with one or more detectable oligo- or polynucleotides, each such oligo- or polynucleotide being complementary to or capable of hybridizing with said nucleic acid of interest or a portion thereof, wherein said oligo- or polynucleotides comprise one or more detectable modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

(i) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

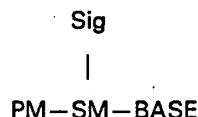
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety or a base analog of any of the foregoing; and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof, and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization;

(ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

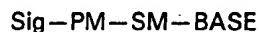
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization; and

(iii) a nucleotide or nucleotide analog, said nucleotide having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,
wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
Sig is covalently attached to PM directly or through a linkage group, and such
covalent attachment does not substantially interfere with double helix formation or
nucleic acid hybridization; and

(b) detecting non-radioactively the presence of said Sig detectable non-
radioactive moieties in any of the detectable oligo- or polynucleotides which have
hybridized to said nucleic acid of interest.

-- 1299. (NEW) The process according to claim 1298, wherein the nucleic acid of
interest comprises DNA, RNA or a DNA-RNA hybrid. --

-- 1300. (NEW) The process according to claim 1298, wherein the nucleic acid of
interest is double-stranded or single-stranded. --

-- 1301. (NEW) The process according to claim 1298, wherein the nucleic acid of
interest has been rendered single-stranded. --

-- 1302. (NEW) The process according to claim 1298, wherein the nucleic acid of
interest is derived from an organism. --

-- 1303. (NEW) The process according to claim 1302, wherein the organism is
selected from the group consisting of prokaryotes and eukaryotes. --

-- 1304. (NEW) The process according to claim 1302, wherein said organism is
selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and
a combination of any of the foregoing. --

-- 1305. (NEW) The process according to claim 1302, wherein said organism is
living. --

-- 1306. (NEW) The process according to claim 1298, wherein the sample is
suspected of containing an etiological agent and the nucleic acid of interest is
naturally associated with the etiological agent. --

- 1307. (NEW) The process according to claim 1306, wherein the sample is of human or animal origin and the etiological agent is selected from the group consisting of bacteria, virus and fungi. --
- 1308. (NEW) The process according to claim 1298, wherein said nucleic acid of interest is derived from a member selected from the group consisting of *Streptococcus pyrogenes*, *Neisseria meningitidis*, *Staphylococcus aureus*, *Candida albicans*, *Pseudomonas aeruginosa*, *Neisseria gonorrhoeae*, *Mycobacterium tuberculosis*, and any combinations of the foregoing. --
- 1309. (NEW) The process according to claim 1298, wherein said one or more oligo- or polynucleotides are derived from *Neisseria gonorrhoeae*. --
- 1310. (NEW) The process according to claim 1298, wherein the sample comprises a bacterium suspected of containing a nucleic acid of interest which imparts resistance to an antibiotic and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the sequence of the bacterium which confers resistance to the antibiotic. --
- 1311. (NEW) The process according to claim 1310, wherein when said bacterium is *Streptococcus pyrogenes* or *Neisseria meningitidis*, said antibiotic is penicillin, wherein when said bacterium is *Staphylococcus aureus*, *Candida albicans*, *Pseudomonas aeruginosa*, *Streptococcus pyrogenes*, or *Neisseria gonorrhoeae*, said antibiotic is a tetracycline, and wherein when said bacterium is *Mycobacterium tuberculosis*, said antibiotic is an aminoglycoside. --
- 1312. (NEW) The process according to claim 1311, wherein said bacterium is *Neisseria gonorrhoeae* and said antibiotic is selected from the group consisting of penicillin, tetracycline, aminoglycoside and combinations thereof. --
- 1313. (NEW) The process according to claim 1298, wherein the sample is suspected of containing a nucleic acid of interest associated with a genetic disorder and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the nucleic acid associated with the genetic disorder. --

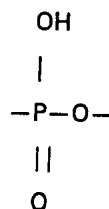
- 1314. (NEW) The process according to claim 1298, wherein the sample is suspected of containing a nucleic acid of interest associated with thalassemia and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the nucleic acid which is absent in the thalassemic subjects. --
- 1315. (NEW) The process according to claim 1298, wherein said process is utilized for chromosomal karyotyping which comprises contacting the sample with a series of the oligo- or polynucleotides which are complementary to a series of known genetic sequences located on chromosomes. --
- 1316. (NEW) The process according to claim 1298, wherein the sample is suspected of containing a nucleic acid which includes a terminal polynucleotide sequence poly A and wherein the oligo- or polynucleotide comprises a modified poly U molecule in which at least one uracil moiety has been modified by chemical addition of Sig to the 5' position of said uracil moiety. --
- 1317. (NEW) The process according to claim 1298, wherein said process is utilized to determine the number of copies of an individual chromosome in a sample. --
- 1318. (NEW) The process according to claim 1298, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme. --
- 1319. (NEW) The process according to claim 1318, wherein said enzyme comprises terminal transferase. --
- 1320. (NEW) The process according to claim 1298, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling. --
1321. (Wholly Rewritten) The process according to claim 1320, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.

- 1322. (NEW) The process according to claim 1320, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase. --
- 1323. (NEW) The process according to claim 1298, wherein said incorporation comprises nick translation. --
- 1324. (NEW) The process according to claim 1298 or 1323, wherein said incorporation is carried out by means of a polymerizing enzyme. --
- 1325. (NEW) The process according to claim 1324, wherein said polymerizing enzyme comprises a polymerase. --
- 1326. (NEW) The process according to claim 1325, wherein said polymerase is selected from the group consisting of DNA polymerase and RNA polymerase. --
- 1327. (NEW) The process according to claim 1298, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a monophosphate, a di-phosphate, a tri-phosphate and a tetra-phosphate. --
- 1328. (NEW) The process according to claim 1298, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise a nucleoside mono-, di- or tri-phosphate. --
- 1329. (NEW) The process according to claim 1298, wherein said sugar moiety or sugar analog comprises a monosaccharide. --
- 1330. (NEW) The process according to claim 1329, wherein said monosaccharide comprises a furanose. --
- 1331. (NEW) The process according to claim 1330, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose. --

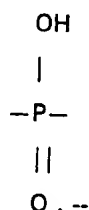
- 1332. (NEW) The process according to claim 1298, wherein said base moiety or base analog BASE in any of said nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --
- 1333. (NEW) The process according to claim 1298, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --
- 1334. (NEW) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to BASE at a position when BASE is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof. --
- 1335. (NEW) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position selected from the group consisting of the N⁴ position when said pyrimidine comprises cytosine, the N² position when said purine comprises adenine or deazaadenine, the N⁶ position when said purine comprises guanine or deazaguanine, and combinations thereof. --
- 1336. (NEW) The process according to claim 1333, wherein in said nucleotide (ii), PM is attached to said monosaccharide or furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 1337. (NEW) The process according to claim 1333, wherein in said nucleotide (iii), PM is attached to said monosaccharide or furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said monosaccharide or furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 1338. (NEW) The process according to claim 1298, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



and



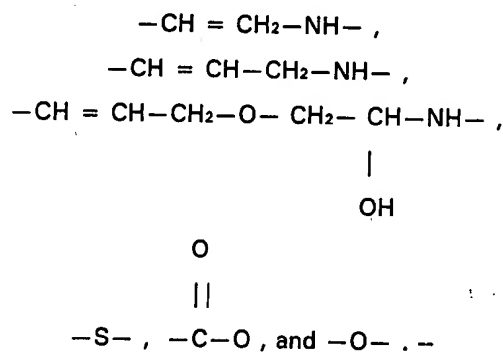
-- 1339. (NEW) The process according to claim 1298, wherein PM is a mono-, di or tri-phosphate, and wherein said nucleotide or nucleotide analog (iii), the Sig detectable non-radioactive moiety is covalently attached to PM through a phosphorus or phosphate oxygen. --

-- 1340. (NEW) The process according to claim 1298, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable signal. --

-- 1341. (NEW) The process according to claim 1298, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $-\text{CH}_2\text{NH}-$ moiety, or both. --

-- 1342. (NEW) The process according to claim 1298, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group. --

-- 1343. (NEW) The process according to claim 1298, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



-- 1344. (NEW) The process according to claim 1298, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety. --

-- 1345. (NEW) The process according to claim 1298, wherein in any of said nucleotides or nucleotide analogs (i), (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group. --

-- 1346. (NEW) The process according to claim 1345, wherein said linkage group contains an amine. --

-- 1347. (NEW) The process according to claim 1346, wherein said amine comprises a primary amine. --

- 1348. (NEW) The process according to claim 1345, wherein said linkage group does not substantially interfere with nucleic acid hybridization or double-stranded nucleic acid formation. --
- 1349. (NEW) The process according to claim 1345, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable signal. --
- 1350. (NEW) The process according to claim 1298, wherein Sig comprises at least three carbon atoms. --
- 1351. (NEW) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --
- 1352. (NEW) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms. --
- 1353. (NEW) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms. --
- 1354. (NEW) The process according to claim 1353, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent. --
- 1355. (NEW) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --
- 1356. (NEW) The process according to claim 1355, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent. --
- 1357. (NEW) The process according to claim 1298, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide. --

- 1358. (NEW) The process according to claim 1298, wherein Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --
- 1359. (NEW) The process according to claim 1358, wherein Sig comprises an electron dense component. --
- 1360. (NEW) The process according to claim 1359, wherein said electron dense component comprises ferritin. --
- 1361. (NEW) The process according to claim 1358, wherein Sig comprises a magnetic component. --
- 1362. (NEW) The process according to claim 1361, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --
- 1363. (NEW) The process according to claim 1361, wherein said magnetic component comprises magnetic beads. --
- 1364. (NEW) The process according to claim 1298, wherein Sig comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein. --
- 1365. (NEW) The process according to claim 1364, wherein the binding protein comprises a lectin. --
- 1366. (NEW) The process according to claim 1365, wherein the lectin comprises concanavalin A. --
- 1367. (NEW) The process according to claim 1365, wherein said lectin is conjugated to ferritin. --
- 1368. (NEW) The process according to claim 1358, wherein Sig comprises an enzyme. --

- 1369. (NEW) The process according to claim 1368, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, β -galactosidase, ribonuclease, glucose oxidase and peroxidase, or a combination thereof. --
- 1370. (NEW) The process according to claim 1358, wherein Sig comprises a hormone. --
- 1371. (NEW) The process according to claim 1358, wherein Sig comprises a metal-containing component. --
- 1372. (NEW) The process according to claim 1371, wherein said metal-containing component is catalytic. --
- 1373. (NEW) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule. --
- 1374. (NEW) The process according to claim 1373, wherein said indicator molecule comprises an aromatic compound. --
- 1375. (NEW) The process according to claim 1374, wherein said aromatic compound is heterocyclic. --
- 1376. (NEW) The process according to claim 1375, wherein said heterocyclic aromatic compound is fluorescent. --
- 1377. (NEW) The process according to claim 1376, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing. --
- 1378. (NEW) The process according to claim 1377, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --
- 1379. (NEW) The process according to claim 1358, wherein Sig comprises a fluorescent component. --

-- 1380. (NEW) The process according to claim 1379, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --

-- 1381. (NEW) The process according to claim 1380, wherein said fluorescent component comprises fluorescein. --

-- 1382. (NEW) The process according to claim 1358 wherein Sig comprises a chemiluminescent component. --

-- 1383. (NEW) The process according to claim 1358, wherein Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component. --

-- 1384. (NEW) The process according to claim 1358, wherein Sig comprises an antibody component. --

-- 1385. (NEW) The process according to claim 1358, wherein Sig comprises a chelating component. --

-- 1386. (NEW) The process according to claim 1373, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, and a chelating component, or a combination of any of the foregoing. --

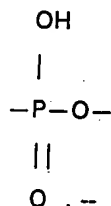
-- 1387. (NEW) The process according to claim 1298, wherein any of nucleotide or nucleotide analogs (i), (ii) and (iii) are detectable by a means selected from the group consisting of a fluorescent measurement and a chemiluminescent measurement, or a combination thereof. --

-- 1388. (NEW) The process according to claim 1298, wherein Sig is detectable non-radioactively when the oligo- or polynucleotide is contained in a double-stranded ribonucleic or deoxyribonucleic acid duplex. --

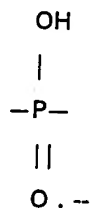
-- 1389. (NEW) The process according to claim 1298, wherein Sig is detectable non-radioactively when it is attached to the nucleotide directly or through a linkage group. --

-- 1390. (NEW) The process according to claim 1389, wherein said linkage group does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal. --

-- 1391. (NEW) The process according to claim 1298, wherein Sig in said nucleotide (iii) is covalently attached to PM via the chemical linkage



-- 1392. (NEW) The process according to claim 1298, wherein Sig in said nucleotide (iii) is covalently attached to PM via the chemical linkage



1393. (Amended) The process according to claim 1298, wherein the [oligo-or] oligo- or polynucleotide is terminally ligated or attached to a polypeptide.

-- 1394. (NEW) The process according to claim 1298, further comprising contacting the sample with a polypeptide capable of forming a complex with Sig and a moiety which can be detected when the complex is formed. --

-- 1395. (NEW) The process according to claims 1393 or 1394, wherein the polypeptide comprises a polylysine. --

- 1396. (NEW) The process according to claims 1393 or 1394, wherein the polypeptide comprises at least one member selected from the group consisting of avidin, streptavidin or anti-Sig immunoglobulin. --
- 1397. (NEW) The process according to claim 1394, wherein Sig comprises a ligand and the polypeptide comprises an antibody thereto. --
- 1398. (NEW) The process according to claim 1394, wherein the moiety which can be detected when the complex is formed is selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --
- 1399. (NEW) The process according to claim 1298, wherein said detecting step is carried out directly. --
- 1400. (NEW) The process according to claim 1399, wherein said direct detection is carried out on one or more nucleotides or nucleotide analogs comprising indicator molecules. --
- 1401. (NEW) The process according to claim 1400, wherein said one or more indicator molecules comprise fluoresceinated nucleotides. --
- 1402. (NEW) The process according to claim 1401, wherein said fluoresceinated nucleotides or nucleotide analogs comprise fluoresceinated DNA. --
- 1403. (NEW) The process according to claim 1298, wherein said detecting step is carried out by means of a directly detectable non-radioactive signal provided by said Sig detectable non-radioactive moiety. --
- 1404. (NEW) The process according to claim 1403, wherein said detecting step the directly detectable non-radioactive signal comprises a member selected from the group consisting of a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound and an electron dense compound. --

-- 1405. (NEW) The process according to claim 1403, wherein said detecting step the directly detectable signal is provided by an enzyme. --

-- 1406. (NEW) The process according to claim 1298, wherein said detecting step is carried out by means of a indirectly detectable non-radioactive signal provided by said Sig detectable non-radioactive moiety. --

-- 1407. (NEW) The process according to claim 1406, wherein said detecting step the indirectly detectable non-radioactive signal is selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme. --

~~DELETED PER 2ND SUPPL. AMEND. 8/31/00 -- 1408. (NEW) The process according to claim 1406, wherein said detecting step the indirectly detectable non-radioactive signal comprises a polynucleotide sequence capable of recognizing a signal containing moiety. --~~

1409. (Wholly Rewritten) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety is capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a phosphorescent measurement, a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

-- 1410. (NEW) The process according to claim 1255, further comprising one or more washing steps. --

1411. (Amended) A process for detecting a nucleic acid of interest in a sample, which process comprises the steps of:

(A) providing:

(i) an oligo- or polynucleotide having two segments:

(a) a first segment complementary to and capable of specifically hybridizing to a portion of said nucleic acid of interest; and

(b) a second segment comprising at least one protein binding nucleic acid sequence; and

(ii) a detectable protein which is capable of binding to said protein binding nucleic acid sequence;

(B) contacting a sample suspected of containing said nucleic acid of interest with said oligo- or polynucleotide (i) and said detectable protein (ii) to form a complex;

(C) detecting non-radioactively the presence of said detectable protein in said complex and said nucleic acid of interest.

-- 1412. (NEW) The process according to claim 1411, wherein the nucleic acid of interest comprises DNA, RNA or a DNA-RNA hybrid. --

-- 1413. (NEW) The process according to claim 1411, wherein the nucleic acid of interest is double-stranded or single-stranded. --

-- 1414. (NEW) The process according to claim 1411, wherein the nucleic acid of interest has been rendered single-stranded. --

-- 1415. (NEW) The process according to claim 1411, wherein the nucleic acid of interest is derived from an organism. --

-- 1416. (NEW) The process according to claim 1415, wherein the living organism is selected from the group consisting of prokaryotes and eukaryotes. --

-- 1417. (NEW) The process according to claim 1415, wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing. --

- 1418. (NEW) The process according to claim 1415, wherein said organism is living. --
- 1419. (NEW) The process according to claim 1411, wherein the sample is suspected of containing an etiological agent and the nucleic acid of interest is naturally associated with the etiological agent. --
- 1420. (NEW) The process according to claim 1419, wherein the sample is of human or animal origin and the etiological agent is selected from the group consisting of bacteria, virus and fungi. --
- 1421. (NEW) The process according to claim 1411, wherein said nucleic acid of interest are derived from a member selected from the group consisting of *Streptococcus pyrogenes*, *Neisseria meningitides*, *Staphylococcus aureus*, *Candida albicans*, *Pseudomonas aeruginosa*, *Neisseria gonorrhoeae*, *Mycobacterium tuberculosis*, and any combinations of the foregoing. --
- 1422. (NEW) The process according to claim 1411, wherein said one or more oligo- or polynucleotides are derived from *Neisseria gonorrhoeae*. --
- 1423. (NEW) The process according to claim 1411, wherein the sample comprises a bacterium suspected of containing a nucleic acid of interest which imparts resistance to an antibiotic and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the sequence of the bacterium which confers resistance to the antibiotic. --
- 1424. (NEW) The process according to claim 1423, wherein when said bacterium is *Streptococcus pyrogenes* or *Neisseria meningitidis*, said antibiotic is penicillin, wherein when said bacterium is *Staphylococcus aureus*, *Candida albicans*, *Pseudomonas aeruginosa*, *Streptococcus pyrogenes*, or *Neisseria gonorrhoea*, said antibiotic is a tetracycline, and wherein when said bacterium is *Mycobacterium tuberculosis*, said antibiotic is an aminoglycoside. --
- 1425. (NEW) The process according to claim 1424, wherein said bacterium is *Neisseria gonorrhoeae* and said antibiotic is selected from the group consisting of penicillin, tetracycline, aminoglycoside and combinations thereof. --

-- 1426. (NEW) The process according to claim 1411, wherein the sample is suspected of containing a nucleic acid of interest associated with a genetic disorder and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the nucleic acid associated with the genetic disorder. --

--1427. (NEW) The process according to claim 1411, wherein the sample is suspected of containing a nucleic acid of interest associated with thalassemia and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the nucleic acid which is absent in the thalassemic subjects. --

-- 1428. (NEW) The process according to claim 1411, wherein said process is utilized for chromosomal karyotyping which comprises contacting the sample with a series of the oligo- or polynucleotides (i) which are complementary to a series of known genetic sequences located on chromosomes. --

-- 1429. (NEW) The process according to claim 1411, wherein said process is utilized to determine the number of copies of an individual chromosome in a sample. --

-- 1430. (NEW) The process according to claim 1411, wherein said at least one protein binding nucleic acid sequence is selected from the group consisting of a promoter, a repressor and an inducer. --

-- 1431. (NEW) The process according to claim 1430, wherein said repressor comprises a lac repressor. --

-- 1432. (NEW) The process according to claim 1411, wherein said at least one protein binding nucleic acid sequence is covalently attached to said oligo- or polynucleotide (i). --

-- 1433. (NEW) The process according to claim 1432, wherein said covalent attachment comprises ligation. --

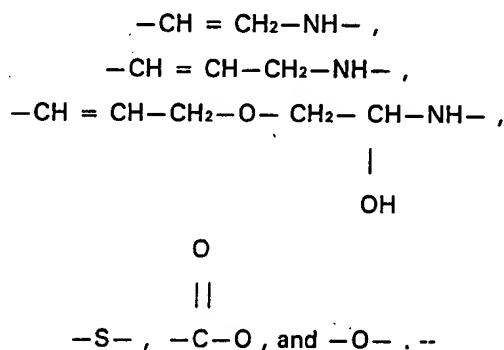
-- 1434. (NEW) The process according to claim 1432, wherein said covalent attachment does not interfere substantially with the characteristic ability of said detectable protein to bind to any hybrid formed between said oligo- or polynucleotide (i) and said nucleic acid of interest. --

--1435. (NEW) The process according to claim 1432, wherein said covalent attachment does not interfere substantially with the characteristic ability of said detectable protein to be detected when bound to any hybrid formed between said oligo- or polynucleotide (i) and said nucleic acid of interest. --

-- 1436. (NEW) The process according to claim 1432, wherein said covalent attachment comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $\text{CH}_2\text{NH}-$ moiety, or both. --

1437. (NEW) The process according to claim 1436, wherein said covalent attachment comprises an allylamine group. --

--1438. (NEW) The process according to claim 1436, wherein said covalent attachment comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



--1439. (NEW) The process according to claim 1432, wherein said covalent attachment includes a glycosidic linkage moiety. --

- 1440. (NEW) The process according to claim 1432, wherein said protein binding sequence is covalently attached to any of the base, phosphate, or sugar moieties in said oligo- or polynucleotide. --
- 1441. (NEW) The process according to claim 1440, wherein said covalent attachment is through a linkage group. --
- 1442. (NEW) The process according to claim 1441, wherein said linkage group contains an amine. --
- 1443. (NEW) The process according to claim 1442, wherein said amine comprises a primary amine. --
- 1444. (NEW) The process according to claim 1441, wherein said linkage group does not substantially interfere with the binding of said non-radioactively detectable protein to said protein binding sequence. --
- 1445. (NEW) The process according to claim 1411, wherein said non-radioactively detectable protein comprises a signaling component or indicator molecule. --
- 1446. (NEW) The process according to claim 1445, wherein said signaling component or indicator molecule comprises at least three carbon atoms. --
- 1447. (NEW) The process according to claim 1446, wherein said signaling component or indicator molecule comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --
- 1448. (NEW) The process according to claim 1446, wherein said signaling component or indicator molecule comprises an aliphatic chemical moiety comprising at least four carbon atoms. --
- 1449. (NEW) The process according to claim 1446, wherein said signaling component or indicator molecule comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms. --

-- 1450. (NEW) The process according to claim 1449, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent. --

-- 1451. (NEW) The process according to claim 1446, wherein said signaling component or indicator molecule comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --

-- 1452. (NEW) The process according to claim 1451, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent. --

1453. (Amended) The process according to claim 1446, wherein said signaling component or indicator molecule comprises a monosaccharide, polysaccharide or an oligosaccharide.

-- 1454. (NEW) The process according to claim 1445, wherein said signaling component or indicator molecule comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --

-- 1455. (NEW) The process according to claim 1445, wherein said signaling component or indicator molecule comprises an aromatic compound. --

-- 1456. (NEW) The process according to claim 1455, wherein said aromatic compound is heterocyclic. --

-- 1457. (NEW) The process according to claim 1456, wherein said heterocyclic aromatic compound is fluorescent. --

-- 1458. (NEW) The process according to claim 1457, wherein said fluorescent heterocyclic aromatic compounds is selected from the group consisting of, fluorescein, rhodamine and dansyl. --

-- 1459. (NEW) The process according to claim 1458, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --

- 1460. (NEW) The process according to claim 1454, wherein said signaling component or indicator molecule comprises a chemiluminescent component. --
- 1461. (NEW) The process according to claim 1454, wherein said signaling component or indicator molecule comprises a chelating component. --
- 1462. (NEW) The process according to claim 1411, wherein said non-radioactively detectable protein is detectable by a means selected from the group consisting of a fluorescent measurement and a chemiluminescent measurement, or a combination thereof. --
- 1463. (NEW) The process according to claim 1411, wherein said non-radioactively detectable protein is detectable when the oligo- or polynucleotide (i) is contained in a double-stranded ribonucleic or deoxyribonucleic acid duplex formed with said nucleic acid of interest. --
- 1464. (NEW) The process according to claim 1411, wherein said nonradioactively detectable protein is detectable when it is attached to said oligo- or polynucleotide (i) directly or through a linkage group. --
- 1465. (NEW) The process according to claim 1411, wherein said oligo- or polynucleotide (i) is contacted with said sample suspected of containing the nucleic acid of interest prior to forming a complex with said non-radioactively detectable protein. --
- 1466. (NEW) The process according to claim 1411, wherein said detecting step is carried out directly. --
- 1467. (NEW) The process according to claim 1466, wherein said direct detection of the non-radioactively detectable protein is carried out on one or more signaling components or indicator molecules. --

-- 1468. (NEW) The process according to claims 1467, wherein said direct detection step is carried out by a member selected from the group consisting of a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound, an enzyme, a radioactive compound and an electron dense compound. --

-- 1469. (NEW) The process according to claim 1411, wherein said detecting step is carried out indirectly. --

1470. (Wholly Rewritten) The process according to claim 1469, wherein said indirect detection is carried out by a means selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme, a compound capable of binding to an insoluble phase, and a combination of any of the foregoing.

1471. (Wholly Rewritten) The process according to claim 1411, wherein said nonradioactively detectable protein is capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a phosphorescent measurement, a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

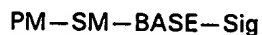
-- 1472. (NEW) The process according to claim 1411, further comprising one or more washing steps. --

-- 1473. (NEW) A process for determining whether the number of copies of a particular chromosome in a cell is normal or abnormal, the process comprising the steps of:

contacting said cell under hybridizing conditions with one or more clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are capable of hybridizing specifically to a locus or loci of said particular chromosome or a portion thereof, wherein said clones or fragments or oligo- or polynucleotides comprise one or more detectable modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or

RNA, and wherein said modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

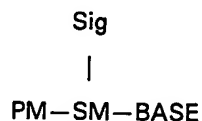
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety or an analog of any of the foregoing thereof, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to the SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof, and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

- (ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

- (iii) a nucleotide or nucleotide analog having the formula

Sig—PM—SM—BASE

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group,

to permit specific hybridization of said clone or clones or DNA fragments or oligo- or polynucleotides to the locus or loci of said particular chromosome;

detecting non-radioactively any specifically hybridized clone or clones or DNA fragments or oligo- or polynucleotides, and determining the number of copies of said particular chromosome; and

comparing said determined number of copies of said particular chromosome with a number of copies of said particular chromosome determined for a normal cell containing said particular chromosome, and determining whether the number of copies of said particular chromosome in said cell is abnormal. --

-- 1474. (NEW) A process for identifying a chromosome of interest in a cell containing other chromosomes, the process comprising the steps of:

providing a set of clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are specifically hybridizable to a locus or loci in said chromosome of interest, wherein said clones or fragments or said oligo- or polynucleotides comprise one or more detectable modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

(i) a nucleotide or nucleotide analog having the formula

PM—SM—BASE—Sig

wherein

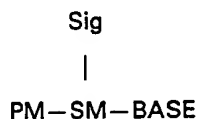
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a detectable non-radioactive moiety, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof, and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

(ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

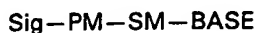
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and
Sig is detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
Sig is covalently attached to PM directly or through a linkage group;

fixing the chromosomes from or in said cell;

contacting said fixed chromosomes under hybridizing conditions with said set
of clones or DNA fragments or oligo- or polynucleotides, permitting specific
hybridization of said set of clones or DNA fragments or oligo- or polynucleotides to
said locus or loci in said chromosome of interest;

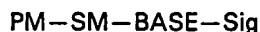
detecting non-radioactively any of said clones or DNA fragments or oligo- or
polynucleotides which have specifically hybridized to said locus or loci in said
chromosome of interest, and obtaining a pattern of hybridizations between said set
of clones or DNA fragments or oligo- or polynucleotides and said chromosomes;
and

identifying said chromosome of interest by means of said hybridization
pattern obtained. --

-- 1475. (NEW) A process for identifying a plurality or all of the chromosomes in a
cell of interest, the process comprising the steps of:

providing sets of clones or DNA fragments, or oligo- or polynucleotides
derived from said clones, wherein said clones or fragments or said oligo- or
polynucleotides are capable of hybridizing specifically to a locus or loci in a
chromosome of said cell of interest, wherein each of said clones or DNA fragments
or oligo- or polynucleotides in said sets are labeled with a different indicator
molecule and each of said clones or DNA fragments or oligo- or polynucleotides
comprises one or more detectable modified or labeled nucleotides or nucleotide
analogs, which nucleotide analogs can be attached to or coupled to or incorporated
into DNA or RNA, and wherein said modified or labeled nucleotide or nucleotide
analog are selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine or a pyrimidine analog, at a position other than the C8 position when BASE is a purine or a purine analog, and at a position other than the C7 position when BASE is a 7-deazapurine or a 7-deazapurine analog thereof;

- (ii) a nucleotide or nucleotide analog having the formula

$$\text{Sig}$$
$$|$$


wherein

PM is a phosphate moiety or phosphate analog,

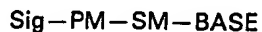
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

- (iii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
Sig is covalently attached to PM directly or through a linkage group;

fixing the chromosomes from or in said cell;

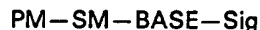
contacting said fixed chromosomes under hybridizing conditions with said
sets of clones or DNA fragments or oligo- or polynucleotides, and permitting
specific hybridization of said sets of clones or DNA fragments or oligo- or
polynucleotides to the locus or loci in said chromosomes; and

detecting non-radioactively any of said different indicator molecules in said
sets of clones or DNA fragments or oligo- or polynucleotides which have
specifically hybridized to the locus or loci in said chromosomes, and identifying any
one of the chromosomes in said cell of interest. --

-- 1476. (NEW) A process for determining the number of chromosomes in an
interphase cell of interest, the process comprising the steps of:

providing sets of clones or DNA fragments or oligo- or polynucleotides
derived from said clones, wherein said set of clones or DNA fragments or oligo- or
polynucleotides are specifically complementary to or specifically hybridizable with
at least one locus or loci in a chromosome of said interphase cell of interest and
each of said clones or DNA fragments or oligo- or polynucleotides in said sets
comprises one or more detectable modified or labeled nucleotides or nucleotide
analogs, which nucleotide analogs can be attached to or coupled to or incorporated
into DNA or RNA, and wherein said modified or labeled nucleotides or nucleotide
analogs are selected from the group consisting of:

(i) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

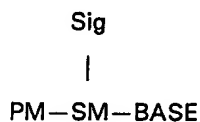
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety or a pyrimidine analog, at a position other than the C8 position when BASE is a purine or a purine analog, and at a position other than the C7 position when BASE is a 7-deazapurine or a 7-deazapurine analog;

(ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

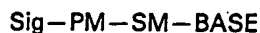
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog, said nucleotide having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is detectable non-radioactive moiety,
wherein PM is covalently attached to the SM, BASE is covalently attached to SM,
and Sig is covalently attached to PM directly or through a linkage group;

contacting said interphase cell under hybridizing conditions with said sets of
clones or DNA fragments or oligo- or polynucleotides, and permitting specific
hybridization of said sets of clones or DNA fragments or oligo- or polynucleotides
to any of the locus or loci in said chromosomes;

detecting non-radioactively any of said sets of clones or DNA fragments or
oligo- or polynucleotides specifically hybridized to the locus or loci in said
chromosomes, to obtain a pattern of generated signals; and comparing each
generated signal with other generated signals in said pattern, and determining the
number of chromosomes in said interphase cell of interest. --

-- 1477. (NEW) The process according to any of claims 1473, 1474, 1475 or
1476, wherein said nucleotide analog can be attached terminally to DNA or RNA by
means of an enzyme. --

-- 1478. (NEW) The process according to claim 1477, wherein said enzyme
comprises terminal transferase. --

-- 1479. (NEW) The process according to any of claims 1473, 1474, 1475 or
1476, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling
means selected from the group consisting of chemical coupling and enzymatic
coupling. --

1480. (Wholly Rewritten) The process according to claim 1479, wherein said
chemical coupling can be carried out by a chemical coupling means selected from
the group consisting of carbodiimide and formaldehyde.

-- 1481. (NEW) The process according to claim 1479, wherein said enzymatic
coupling can be carried out by an enzymatic coupling means selected from the
group consisting of DNA ligase and RNA ligase. --

- 1482. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said incorporation comprises nick translation. --
- 1483. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said incorporation is carried out by means of a polymerizing enzyme. --
- 1484. (NEW) The process according to claim 1483, wherein said polymerizing enzyme comprises a polymerase. --
- 1485. (NEW) The process according to claim 1484, wherein said polymerase is selected from the group consisting of DNA polymerase and RNA polymerase. --
- 1486. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a mono-phosphate, a di-phosphate, a tri-phosphate and a tetraphosphate. --
- 1487. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise nucleoside mono-, di- or tri-phosphate. --
- 1488. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said sugar moiety or sugar analog comprises a monosaccharide. --
- 1489. (NEW) The process according to claim 1488, wherein said monosaccharide comprises a furanose. --
- 1490. (NEW) The process according to claim 1489, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose. --
- 1491. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said base moiety or base analog BASE in any of said nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --

-- 1492. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --

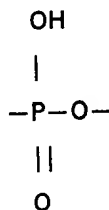
-- 1493. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to BASE at a position when BASE is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof. --

-- 1494. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position selected from the group consisting of the N⁴ position when said pyrimidine comprises cytosine, the N² position when said purine comprises adenine or deazaadenine, the N⁶ position when said purine comprises guanine or deazaguanine, and combinations thereof. --

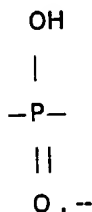
-- 1495. (NEW) The process according to claim 1489, wherein in said nucleotide (ii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 1496. (NEW) The process according to claim 1489, wherein in said nucleotide (iii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 1497. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



and



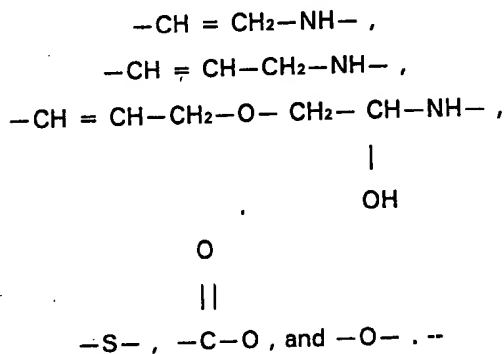
-- 1498. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein PM is a mono-, di or tri-phosphate, and wherein said nucleotide or nucleotide analog (iii), the Sig moiety is covalently attached to PM through a phosphorus or phosphate oxygen. --

-- 1499. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable signal. --

-- 1500. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $-\text{CH}_2\text{NH}-$ moiety, or both. --

-- 1501. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group. --

-- 1502. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



-- 1503. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety. --

-- 1504. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein in any of said nucleotides or nucleotide analogs (i), (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group. --

-- 1505. (NEW) The process according to claim 1504, wherein said linkage group contains an amine. --

- 1506. (NEW) The process according to claim 1505, wherein said amine comprises a primary amine. --
- 1507. (NEW) The process according to claim 1504, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable signal. --
- 1508. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises at least three carbon atoms. --
- 1509. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --
- 1510. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms. --
- 1511. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms. --
- 1512. (NEW) The process according to claim 1511, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent. --
- 1513. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --
- 1514. (NEW) The process according to claim 1513, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent. --
- 1515. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide. --

-- 1516. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --

-- 1517. (NEW) The process according to claim 1516, wherein Sig comprises an electron dense component. --

-- 1518. (NEW) The process according to claim 1516, wherein said electron dense component comprises ferritin. --

-- 1519. (NEW) The process according to claim 1516, wherein Sig comprises a magnetic component. --

-- 1520. (NEW) The process according to claim 1519, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --

-- 1521. (NEW) The process according to claim 1519, wherein said magnetic component comprises magnetic beads. --

-- 1522. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises a sugar residue and the sugar residue is completed with or attached to a sugar binding protein or a polysaccharide binding protein. --

-- 1523. (NEW) The process according to claim 1522, wherein the binding protein comprises a lectin. --

-- 1524. (NEW) The process according to claim 1523, wherein the lectin comprises concanavalin A. --

-- 1525. (NEW) The process according to claim 1523, wherein said lectin is conjugated to ferritin. --

- 1526. (NEW) The process according to claim 1516, wherein Sig comprises an enzyme. --
- 1527. (NEW) The process according to claim 1526, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, galactosidase, ribonuclease, glucose oxidase and peroxidase, or a combination thereof. --
- 1528. (NEW) The process according to claim 1516, wherein Sig comprises a hormone. --
- 1529. (NEW) The process according to claim 1516, wherein Sig comprises a metal-containing component. --
- 1530. (NEW) The process according to claim 1529, wherein said metal-containing component is catalytic. --
- 1531. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule. --
- 1532. (NEW) The process according to claim 1531, wherein said indicator molecule comprises an aromatic compound. --
- 1533. (NEW) The process according to claim 1532, wherein said aromatic compound is heterocyclic. --
- 1534. (NEW) The process according to claim 1533, wherein said heterocyclic aromatic compound is fluorescent. --
- 1535. (NEW) The process according to claim 1534, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing. --
- 1536. (NEW) The process according to claim 1535, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --

- 1537. (NEW) The process according to claim 1516, wherein Sig comprises a fluorescent component. --
- 1538. (NEW) The process according to claim 1537, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --
- 1539. (NEW) The process according to claim 1538, wherein said fluorescent component comprises fluorescein. --
- 1540. (NEW) The process according to claim 1516, wherein Sig comprises a chemiluminescent component. --
- 1541. (NEW) The process according to claim 1516, wherein Sig comprises an antigenic or hapten component capable of completing with an antibody specific to the component. --
- 1542. (NEW) The process according to claim 1516, wherein Sig comprises an antibody component. --
- 1543. (NEW) The process according to claim 1516, wherein Sig comprises a chelating component. --
- 1544. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule. --
- 1545. (NEW) The process according to claim 1544, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, and a chelating component, or a combination of any of the foregoing. --

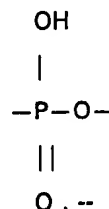
-- 1546. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein any of nucleotide or nucleotide analogs (i), (ii) and (iii) are detectable by a means selected from the group consisting of a fluorescent measurement and a chemiluminescent measurement, or a combination thereof. --

-- 1547. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig is detectable when the oligo- or polynucleotide is contained in a double-stranded ribonucleic or deoxyribonucleic acid duplex. --

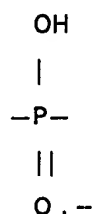
-- 1548. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig is detectable when it is attached to the nucleotide directly or through a linkage group. --

-- 1549. (NEW) The process according to claim 1548, wherein said linkage group does not interfere substantially with the characteristic ability of Sig to form a detectable signal. --

--1550. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig in said nucleotide (iii) is covalently attached to PM via the chemical linkage



-- 1551. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig in said nucleotide (iii) is covalently attached to PM via the chemical linkage



- 1552. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein the oligo-or polynucleotide is terminally ligated or attached to a polypeptide. --
- 1553. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, further comprising contacting the sample with a polypeptide capable of forming a complex with Sig and a moiety which can be detected when the complex is formed. --
- 1554. (NEW) The process according to claim 1552, wherein the polypeptide comprises a polylysine. --
- 1555. (NEW) The process according to claim 1553, wherein the polypeptide comprises a polylysine. --
- 1556. (NEW) The process according to claim 1552, wherein the polypeptide comprises at least one member selected from the group consisting of avidin, streptavidin or anti-Sig immunoglobulin. --
- 1557. (NEW) The process according to claim 1553, wherein the polypeptide comprises at least one member selected from the group consisting of avidin, streptavidin or anti-Sig immunoglobulin. --
- 1558. (NEW) The process according to claim 1553, wherein Sig comprises a ligand and the polypeptide comprises an antibody thereto. --
- 1559. (NEW) The process according to claim 1553, wherein the moiety which can be detected when the complex is formed is selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --
- 1560. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said detecting step is carried out directly. --

-- 1561. (NEW) The process according to claim 1560, wherein said direct detection is carried out on one or more indicator molecules. --

--1562. (NEW) The process according to claim 1561, wherein said one or more indicator molecules comprise fluoresceinated nucleotides. --

-- 1563. (NEW) The process according to claim 1562, wherein said fluoresceinated nucleotides or nucleotide analogs comprise fluoresceinated DNA. --

-- 1564. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said detecting step is carried out by means of a directly detectable signal provided by said Sig detectable non-radioactive moiety. --

-- 1565. (NEW) The process according to claim 1564, wherein said detecting step is carried out by means of a member selected from the group consisting of a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a cherniluminescent compound and an electron dense compound. --

-- 1566. (NEW) The process according to claim 1564, wherein said detecting step the directly -detectable signal is provided by an enzyme. --

-- 1567. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said detecting step is carried out by means of a indirectly detectable signal provided by said Sig detectable non-radioactive moiety. --

-- 1568. (NEW) The process according to claim 1567, wherein said detecting step the indirectly detectable non-radioactive signal is provided by a member selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme. --

~~DELETED PER 2ND SUPPL. AMEND. 8/31/00 --1569. (NEW) The process according to claim 1567, wherein said detecting step the indirectly detectable non-radioactive signal is provided by a polynucleotide sequence capable of recognizing a signal containing moiety.~~

1570. (Wholly Rewritten) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety is capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a phosphorescent measurement, a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

-- 1571. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, further comprising one or more washing steps. --

1572. (Wholly Rewritten) The process according to claim 1473, 1474, 1475 or 1476, wherein said one or more clones or DNA fragments or oligo- or polynucleotides derived from clone or clones are derived from said particular chromosome or said chromosome of interest or said chromosome in said interphase cell of interest.

1573. (Amended) The process according to claim 1475, wherein each of [said.] said set of clones or DNA fragments or oligo- or polynucleotides is labeled with the same indicator molecule.

-- 1574. (NEW) The process according to any of claims. 1473, 1474 or 1475, wherein said detecting step is carried out by a means selected from the group consisting of manual means and automatic means. --

-- 1575. (NEW) The process according to claim 1574, wherein said manual means comprises visualization. --

-- 1576. (NEW) The process according to claim 1574, wherein said automatic means comprises computerized automatic karyotyping. --

-- 1577. (NEW) The process according to claim 1476, wherein each of said sets of clones or DNA fragments or oligo- or polynucleotides is labeled with the same indicator molecule. --

-- 1578. (NEW) The process according to claim 1476, wherein each of said sets of clones or DNA fragments or oligo- or polynucleotides is labeled with a different indicator molecule. --

-- 1579. (NEW) The process according to claim 1476, wherein said detecting and determining step is carried out by a means selected from the group consisting of manual means and automatic means. --

-- 1580. (NEW) The process according to claim 1579, wherein said manual means comprises visualization. --

-- 1581. (NEW) The process according to claim 1579, wherein said automatic means comprises computerized automatic karyotyping. --

1582. (Amended) A process for preparing a detectable non-radioactively labeled oligo- or polynucleotide of interest, comprising the steps of:

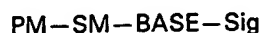
(A) providing either:

(1) one or more detectable chemically modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA or an oligo- or polynucleotide of interest, alone or in conjunction with one or more other modified or unmodified nucleic acids selected from the group consisting of nucleotides, oligonucleotides and polynucleotides, wherein said other modified or unmodified nucleic acids are capable of incorporating into an oligo- or polynucleotide of interest, and wherein said chemically modified or labeled nucleotides or nucleotide analogs comprise one or more signaling moieties which are capable of providing directly or indirectly a detectable non-radioactive signal; or

(2) an oligo- or polynucleotide of interest comprising one or more said detectable chemically modified or labeled nucleotides or nucleotide analogs, alone or in conjunction with one or more other modified or unmodified nucleic acids selected from the group consisting of nucleotides, oligonucleotides and polynucleotides;

wherein said chemically modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate moiety, the base moiety or the base analog, and are selected from the group consisting of:

(i)



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a detectable non-radioactive moiety, and

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof, and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

(ii)

Sig

|



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a detectable non-radioactive moiety, and

wherein said PM is covalently attached to SM, said BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii)

Sig—PM—SM—BASE

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

[Sig.] Sig is detectable non-radioactive moiety; and

wherein PM is covalently attached to SM, BASE is covalently attached SM, and Sig is covalently attached to PM directly or through a linkage group; and

said oligo- or polynucleotide of interest; and

(B) either incorporating said one or more modified or labeled nucleotides or nucleotide analogs (A)(1) into said oligo- or polynucleotide, and preparing a labeled oligo- or polynucleotide of interest, or preparing said oligo- or polynucleotide of interest from said oligo- or polynucleotide recited in step (A)(2) above.

-- 1583. (NEW) The process according to claim 1582, wherein said oligo- or polynucleotide of interest is derived from an organism. --

-- 1584. (NEW) The process according to claim 1583, wherein said organism is living. --

-- 1585. (NEW) The process according to claims 1583 or 1584, wherein the organism is selected from the group consisting of prokaryotes and eukaryotes. --

-- 1586. (NEW) The process according to claim 1585, wherein said organism comprises a eukaryote. --

- 1587. (NEW) The process according to claim 1586, wherein said eukaryotic oligo- or polynucleotide of interest is contained within a chromosome. --
- 1588. (NEW) The process according to claim 1586, wherein said eukaryote comprises a mammal. --
- 1589. (NEW) The process according to claim 1588, wherein said mammalian oligo- or polynucleotide of interest is contained within a chromosome. --
- 1590. (NEW) The process according to claim 1588, wherein said mammal comprises a human being. --
- 1591. (NEW) The process according to claim 1590, wherein said human oligo- or polynucleotide of interest is contained within a chromosome. --
- 1592. (NEW) The process according to claim 1591, wherein said human chromosomal oligo- or polynucleotide of interest is part of a human gene library. --
- 1593. (NEW) The process according to claim 1592, wherein said living organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing. --
- 1594. (NEW) The process according to claim 1584, wherein said living organism comprises a mammal. --
- 1595. (NEW) The process according to claim 1594, wherein said mammal comprises a human being. --
- 1596. (NEW) The process according to claim 1582, wherein said incorporating step is carried out using an enzyme. --
- 1597. (NEW) The process according to claim 1596, wherein said enzyme comprises a polymerase. --
- 1598. (NEW) The process according to claim 1597, wherein said polymerase comprises DNA polymerase. --

-- 1599. (NEW) The process according to claim 1582, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme. --

-- 1600. (NEW) The process according to claim 1599, wherein said enzyme comprises terminal transferase. --

-- 1601. (NEW) The process according to claim 1582, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling. --

1602. (Wholly Rewritten) The process according to claim 1601, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.

-- 1603. (NEW) The process according to claim 1601, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase. --

-- 1604. (NEW) The process according to claim 1582, wherein said incorporation comprises nick translation. --

-- 1605. (NEW) The process according to claim 1582 or 1604, wherein said incorporation is carried out by means of a polymerizing enzyme. --

-- 1606. (NEW) The process according to claim 1605, wherein said polymerizing enzyme comprises a polymerase. --

-- 1607. (NEW) The process according to claim 1606, wherein said polymerase is selected from the group consisting of DNA polymerase and RNA polymerase. --

-- 1608. (NEW) The process according to claim 1582, wherein said one or more chemically modified nucleotides or said other modified or unmodified nucleic acids comprise a nucleoside di- or tri-phosphate. --

-- 1609. (NEW) The process according to claim 1582, wherein said incorporating step is template dependent or template independent. --

-- 1610. (NEW) The process according to claim 1609, wherein said incorporating step is template dependent. --

1611. (Wholly Rewritten) The process according to claim 1582, wherein said labeled oligo- or polynucleotide of interest prepared by said incorporating step comprises at least one internal modified nucleotide.

-- 1612. (NEW) The process according to claim 1582, wherein said labeled oligo- or polynucleotide of interest prepared by said incorporating step comprises at least one terminal modified nucleotide. --

~~DELETED PER 2ND SUPPL. AMEND. 8/31/00 -- 1613. (NEW) The process according to claim 1582, wherein said labeled oligo- or polynucleotide prepared by said incorporating step comprises at least one internal modified nucleotide and at least one terminal modified nucleotide. --~~

-- 1614. (NEW) The process according to claim 1582, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a monophosphate, a di-phosphate, a tri-phosphate and a tetra-phosphate. --

-- 1615. (NEW) The process according to claim 1582, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise a nucleoside mono-, di- or tri-phosphate. --

-- 1616. (NEW) The process according to claim 1582, wherein said sugar moiety or sugar analog comprises a monosaccharide. --

-- 1617. (NEW) The process according to claim 1616, wherein said monosaccharide comprises a furanose. --

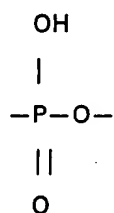
-- 1618. (NEW) The process according to claim 1617, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose. --

- 1619. (NEW) The process according to claim 1582, wherein in said chemically modified nucleotides or nucleotide analogs (i) Sig is covalently attached to said BASE at a position when BASE is a pyrimidine or pyrimidine analog that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to BASE at a position when BASE is a purine or purine analog that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof. --
- 1620. (NEW) The process according to claim 1582, wherein in said chemically modified nucleotides or nucleotide analogs (i) Sig is covalently attached to said BASE at a position selected from the group consisting of the N⁴ position when said pyrimidine or pyrimidine analog comprises cytosine or a cytosine analog, the N² position when said purine or purine analog comprises adenine, an adenine analog, or deazaadenine, the N⁶ position when said purine comprises guanine or deazaguanine, and combinations thereof. --
- 1621. (NEW) The process according to claim 1582, wherein said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) or both is selected from the group consisting of a pyrimidine, a pyrimidine analog, a purine, a purine analog, a 7-deazapurine, a 7-deazapurine analog, and a combination of any of the foregoing. --
- 1622. (NEW) The process according to claim 1582, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) or both is selected from the group consisting of a pyrimidine, a pyrimidine analog, a purine, a purine analog, a 7-deazapurine, a 7-deazapurine analog, and a combination of any of the foregoing. --
- 1623. (NEW) The process according to claim 1582, wherein in said incorporating step, Sig in the nucleotide (i) is covalently attached to BASE through a linkage group. --

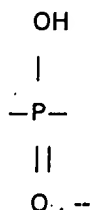
- 1624. (NEW) The process according to claim 1623, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable signal. --
- 1625. (NEW) The process according to claim 1623, wherein said linkage group contains an amine. --
- 1626. (NEW) The process according to claim 1625, wherein said amine comprises a primary amine. --
- 1627. (NEW) The process according to claim 1582, wherein in said incorporating step, Sig in the nucleotide (ii) is covalently attached to SM through a linkage group. --
- 1628. (NEW) The process according to claim 1627, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable signal. --
- 1629. (NEW) The process according to claim 1627, wherein said linkage group contains an amine. --
- 1630. (NEW) The process according to claim 1629, wherein said amine comprises a primary amine. --
- 1631. (NEW) The process according to claim 1582, wherein in said incorporating step, Sig in the nucleotide (iii) is covalently attached to PM through a linkage group. --
- 1632. (NEW) The process according to claim 1631, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable signal. --
- 1633. (NEW) The process according to claim 1631, wherein said linkage group contains an amine. --

- 1634. (NEW) The process according to claim 1633, wherein said amine comprises a primary amine. --
- 1635. (NEW) The process according to claim 1617, wherein in said nucleotide (ii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or a pyrimidine analog, or the N9 position when BASE is a purine, a purine analog, 7-deazapurine, or a 7-deazapurine analog, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --
- 1636. (NEW) The process according to claim 1617, wherein in said nucleotide (iii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or a pyrimidine analog, or the N9 position when BASE is a purine, a purine analog, 7-deazapurine, or a 7-deazapurine analog, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 1637. (NEW) The process according to claim 1582, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



and



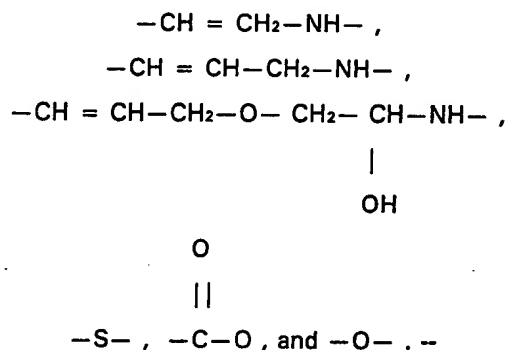
-- 1638. (NEW) The process according to claim 1582, wherein PM is a mono-, di or tri-phosphate, and wherein in said nucleotide or nucleotide analog (iii), the Sig moiety is covalently attached to PM through a phosphorus or phosphate oxygen. --

-- 1639. (NEW) The process according to claim 1582, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable signal. --

-- 1640. (NEW) The process according to claim 1582, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $\text{--CH}_2\text{NH--}$ moiety, or both. --

-- 1641. (NEW) The process according to claim 1582, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group. --

-- 1642. (NEW) The process according to claim 1582, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



--1643. (NEW) The process according to claim 1582, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety. --

-- 1644. (NEW) The process according to claim 1582, wherein in said nucleotides or nucleotide analogs (i), (ii) or (iii), Sig is covalently attached to BASE, SM or PM through a linkage group. --

-- 1645. (NEW) The process according to claim 1644, wherein said linkage group contains an amine. --

-- 1646. (NEW) The process according to claim 1645, wherein said amine comprises a primary amine. --

-- 1647. (NEW) The process according to claim 1645, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable signal. --

-- 1648. (NEW) The process according to claim 1582, wherein said Sig comprises at least three carbon atoms. --

- 1649. (NEW) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --
- 1650. (NEW) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms. --
- 1651. (NEW) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms. --
- 1652. (NEW) The process according to claim 1651, wherein said heterocyclic aromatic compound is fluorescent. --
- 1653. (NEW) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --
- 1654. (NEW) The process according to claim 1653, wherein said heterocyclic aromatic compound is fluorescent. --
- 1655. (NEW) The process according to claim 1582, wherein said Sig comprises a monosaccharide, polysaccharide or an oligosaccharide. --
- 1656. (NEW) The process according to claim 1582, wherein said Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --
- 1657. (NEW) The process according to claim 1656, wherein said Sig comprises an electron dense component. --

- 1658. (NEW) The process according to claim 1657, wherein said electron dense component comprises ferritin. --
- 1659. (NEW) The process according to claim 1656, wherein said Sig comprises a magnetic component. --
- 1660. (NEW) The process according to claim 1659, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --
- 1661. (NEW) The process according to claim 1659, wherein said magnetic component comprises magnetic beads. --
- 1662. (NEW) The process according to claim 1582, wherein said Sig comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein. --
- 1663. (NEW) The process according to claim 1662, wherein the binding protein comprises a lectin. --
- 1664. (NEW) The process according to claim 1663, wherein the lectin comprises concanavalin A. --
- 1665. (NEW) The process according to claim 1663, wherein said lectin is conjugated to ferritin. --
- 1666. (NEW) The process according to claim 1656, wherein said Sig comprises an enzyme. --
- 1667. (NEW) The process according to claim 1666, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, galactosidase, ribonuclease, glucose oxidase and peroxidase, or a combination thereof. --
- 1668. (NEW) The process according to claim 1656, wherein said Sig comprises a hormone. --

- 1669. (NEW) The process according to claim 1656, wherein said Sig comprises a metal-containing component. --
- 1670. (NEW) The process according to claim 1669, wherein said metal-containing component is catalytic. --
- 1671. (NEW) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule. --
- 1672. (NEW) The process according to claim 1671, wherein said indicator molecule comprises an aromatic compound. --
- 1673. (NEW) The process according to claim 1672, wherein said aromatic compound is heterocyclic. --
- 1674. (NEW) The process according to claim 1673, wherein said heterocyclic aromatic compound is fluorescent. --
- 1675. (NEW) The process according to claim 1674, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine and dansyl. --
- 1676. (NEW) The process according to claim 1675, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --
- 1677. (NEW) The process according to claim 1671, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, and a chelating component, or a combination of any of the foregoing. --
- 1678. (NEW) The process according to claim 1656, wherein said Sig comprises a fluorescent component. --
- 1679. (NEW) The process according to claim 1678, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --

- 1680. (NEW) The process according to claim 1679, wherein said fluorescent component comprises fluorescein. --
- 1681. (NEW) The process according to claim 1656, wherein said Sig comprises a chemiluminescent component. --
- 1682. (NEW) The process according to claim 1656, wherein said Sig comprises an antigenic or hapten component capable of completing with an antibody specific to the component. --
- 1683. (NEW) The process according to claim 1656, wherein said Sig comprises an antibody component. --
- 1684. (NEW) The process according to claim 1656, wherein said Sig comprises a chelating component. --
- 1685. (NEW) The process according to claim 1582, wherein any of nucleotide or nucleotide analogs (i), (ii) and (iii) are detectable by a means selected from the group consisting of a fluorescent measurement and a chemiluminescent measurement, or a combination thereof. --
- 1686. (NEW) The process according to claim 1582, wherein said Sig is detectable when the oligo- or polynucleotide is contained in a double-stranded ribonucleic or deoxyribonucleic acid duplex. --
- 1687. (NEW) The process according to claim 1582, wherein said Sig is detectable when it is attached to the nucleotide directly or through a linkage group. --
- 1688. (NEW) The process according to claim 1687, wherein said linkage group does not interfere substantially with the characteristic ability of Sig to form a detectable signal. --

1689. (Wholly Rewritten) The process according to claim 1582, wherein said labeled oligo- or polynucleotide of interest is terminally ligated or attached to a polypeptide.

-- 1690. (NEW) The process according to claim 1689, further comprising contacting the sample with a polypeptide capable of forming a complex with Sig and a moiety which can be detected when the complex is formed. --

-- 1691. (NEW) The process according to claim 1689, wherein the polypeptide comprises a polylysine. --

-- 1692. (NEW) The process according to claim 1689, wherein the polypeptide comprises at least one member selected from the group consisting of avidin, streptavidin or anti-Sig immunoglobulin. --

1693. (Amended) The process according to claim 1690, wherein said Sig comprises a ligand [and.] and the polypeptide comprises an antibody thereto.

-- 1694. (NEW) The process according to claim 1690, wherein the moiety which can be detected when the complex is formed is selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --

-- 1695. (NEW) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety is capable of being directly detected. --

-- 1696. (NEW) The process according to claim 1695, wherein said directly detectable signal providing Sig detectable non-radioactive moiety is selected from the group consisting of a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound, an electron dense compound and an enzyme. --

-- 1697. (NEW) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety is capable of being indirectly detected. --

1698. (Wholly Rewritten) The process according to claim 1697, wherein said detecting step the indirectly detectable signal is provided by a member selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme and a combination of any of the foregoing.

1699. (Wholly Rewritten) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety is capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a phosphorescent measurement, a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

-- 1700. (NEW) A process for determining the sequence of a nucleic acid of interest, comprising the steps of:

providing or generating labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or a portion thereof, wherein each of said fragments comprises one or more detectable modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, wherein said modified or labeled nucleotides or nucleotide analogs comprise one or more chelating compounds or chelating components capable of providing a detectable radioactive signal, and wherein said one or more modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety, or the base analog thereof;

subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments; and

detecting the presence of each of said separated or resolved fragments by means of the detectable radioactive signal provided by said chelating compounds or chelating components in the modified or labeled nucleotides or nucleotide analogs, and determining the sequence of said nucleic acid of interest. --

1701. (Amended) A process for determining the sequence of a nucleic acid of interest, comprising the steps of:

providing or generating detectable labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, wherein said modified or labeled nucleotides or nucleotide analogs comprise one or more chelating compounds or chelating components capable of providing a detectable radioactive signal, and wherein said one or more modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety, or the base analog thereof;

introducing or subjecting said fragments to a sequencing gel;

separating or resolving said fragments in said sequencing gel; and

detecting each of the separated or resolved fragments by means of the detectable radioactive signal provided by said chelating compounds or chelating components in the modified or labeled nucleotides or nucleotide analogs, and determining the sequence of said nucleic acid of interest.

1702. (Amended) A process for determining the sequence of a nucleic acid of interest, comprising the steps of:

providing or generating detectable labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, wherein said modified or labeled nucleotides or nucleotide analogs comprise one or more chelating compounds or chelating components capable of providing a detectable radioactive signal, and wherein said one or more modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety or the base analog thereof;

detecting the detectable labeled nucleic acid fragments with a sequencing gel; and

determining the sequence of said nucleic acid of interest.

1703. (Amended) A process for determining the sequence of a nucleic acid of interest, comprising the step of detecting with a sequencing gel one or more detectable labeled nucleic acid fragments comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, wherein said modified or labeled nucleotides or nucleotide analogs comprise one or more chelating compounds or chelating components capable of providing a detectable radioactive signal, and wherein said one or more modified nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the base moiety or the base analog thereof.

1704. (Amended) A process for determining in a sequencing gel the presence of nucleic acid fragments comprising a sequence complementary to a nucleic acid sequence of interest or a portion thereof, said process comprising the steps of:

(A) providing

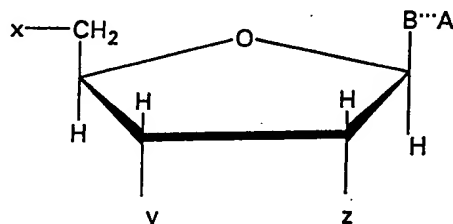
(i) one or more detectable chemically modified nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into a nucleic acid, or

(ii) one or more oligonucleotides or polynucleotides comprising at least one of said detectable chemically modified nucleotides or nucleotide analogs; or

(iii) both (i) and (ii);

wherein said chemically modified nucleotides or nucleotide analogs (i) and said oligonucleotides and polynucleotides (ii) are capable of attaching to or coupling to or incorporating into or forming one or more nucleic acid fragments, wherein said detectable chemically modified nucleotides or nucleotide analogs comprise one or more chelating compounds or chelating components capable of providing a detectable radioactive signal, and wherein said chemically modified nucleotides or nucleotide analogs have been modified non-disruptively or disruptively on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety or the base analog thereof; and;

(B) incorporating said one or more chemically modified nucleotides or nucleotide analogs (i) or said one or more oligonucleotides or polynucleotides comprising at least one of said chemically modified or labeled nucleotides (ii), or both (i) and (ii), into said one or more nucleic acid fragments, to prepare detectable labeled fragments, each such fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, said labeled fragments further comprising one or more chemically modified nucleotides or nucleotide analogs selected from the group consisting of:

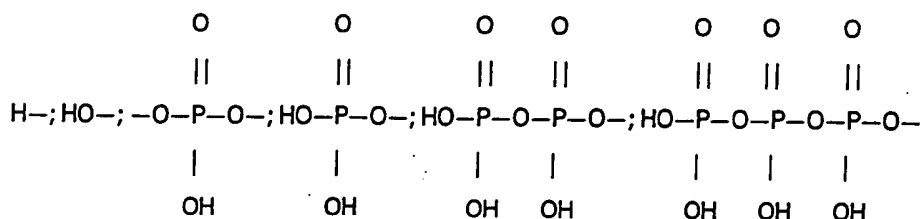


wherein B represents a purine moiety, a 7-deazapurine moiety, a pyrimidine moiety, or an analog of any of the foregoing, and B is covalently bonded to the C1'-position of the sugar moiety or sugar analog, provided that whenever B is a purine, a purine analog, a 7-deazapurine moiety or a 7-deazapurine analog, the sugar moiety or sugar analog is attached at the N9 position of the purine moiety, the purine analog, the, 7-deazapurine moiety or the 7-analog thereof, and whenever B is a pyrimidine moiety or a pyrimidine analog, the sugar moiety or sugar analog is attached at the N1 position of the pyrimidine moiety or the pyrimidine analog;

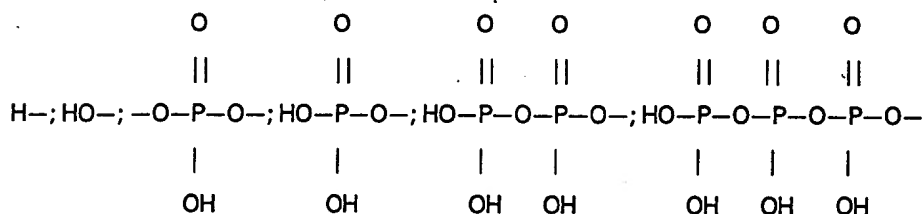
wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety comprising a chelating compound or chelating component capable of providing directly or indirectly a detectable radioactive signal; and

wherein B and A are covalently attached directly or through a linkage group, and

wherein x comprises a member selected from the group consisting of:



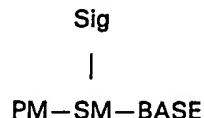
wherein y comprises a member selected from the group consisting of:



wherein z comprises a member selected from the group consisting of

H- and HO- [--]

(ii)



wherein

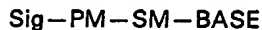
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of providing a detectable radioactive signal, and wherein said PM is covalently attached to SM, said BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii)



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of providing a detectable radioactive signal; and

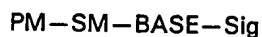
wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
Sig is covalently attached to PM directly or through a linkage group;

- (C) transferring or subjecting said labeled fragments to a sequencing gel;
- (D) separating or resolving said labeled fragments; and
- (E) detecting directly or indirectly the presence of said labeled fragments.

-- 1705. (NEW) A process for detecting a nucleic acid of interest in a sample,
which process comprises the steps of:

- (a) specifically hybridizing said nucleic acid of interest in the sample with one or more oligo- or polynucleotides, each such oligo- or polynucleotide being complementary to or capable of hybridizing with said nucleic acid of interest or a portion thereof, wherein said oligo- or polynucleotides comprise one or more detectable modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

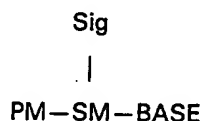
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety or a base analog of any of the foregoing; and

Sig is a signaling moiety comprising a chelating compound or component capable of providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the

C8 position when BASE is a purine moiety or an analog thereof and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof, and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization;

(ii) a nucleotide or nucleotide analog having the formula



wherein

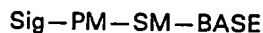
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or component capable of providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization; and

(iii) a nucleotide or nucleotide analog, said nucleotide having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or components capable of providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group, and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization; and

(b) detecting radioactively the presence of said signaling moieties Sig in any of the oligo- or polynucleotides which have hybridized to said nucleic acid of interest. --

-- 1706. (NEW) A process for detecting a nucleic acid of interest in a sample, which process comprises the steps of:

(A) providing:

- (i) an oligo- or polynucleotide having two segments:
 - (a) a first segment complementary to and capable of hybridizing to a portion of said nucleic acid of interest; and
 - (b) a second segment comprising at least one protein binding sequence; and
- (ii) a protein capable of binding to said protein binding sequence and comprising a chelating compound or chelating component capable of providing a detectable radioactive signal;

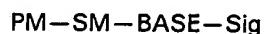
(B) contacting a sample suspected of containing said nucleic acid of interest with said oligo- or polynucleotide (ii) and said detectable protein (iii) to form a complex;

(C) detecting radioactively the presence of said protein in said complex and said nucleic acid of interest. --

1707. (Wholly Rewritten) A process for determining whether the number of copies of a particular chromosome in a cell is normal or abnormal, the process comprising the steps of:

contacting said cell under hybridizing conditions with one or more clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are capable of hybridizing specifically to a locus or loci of said particular chromosome or a portion thereof, wherein said clones or fragments or oligo- or polynucleotides comprise one or more detectable modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula



wherein

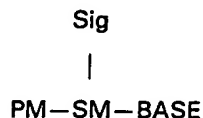
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety or an analog of any of the foregoing thereof, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of providing a detectable radioactive signal, wherein PM is covalently attached to the SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof, and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

- (ii) a nucleotide or nucleotide analog having the formula



wherein

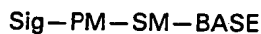
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group, to permit specific hybridization of said clone or clones or DNA fragments or oligo- or polynucleotides to the locus or loci of said particular chromosome;

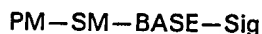
detecting radioactively the signal generated by said specifically hybridized clone or clones or DNA fragments or oligo- or polynucleotides, and determining the number of copies of said particular chromosome; and

comparing said determined number of copies of said particular chromosome with a number of copies of said particular chromosome determined for a normal cell containing said particular chromosome, and determining whether the number of copies of said particular chromosome in said cell is abnormal.

-- 1708. (NEW) A process for identifying a chromosome of interest in a cell containing other chromosomes, the process comprising the steps of:

providing a set of clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are specifically hybridizable to a locus or loci in said chromosome of interest, wherein said clones or fragments or oligo- or polynucleotides comprise one or more detectable modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula



wherein

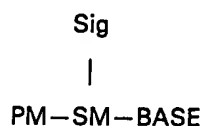
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof, and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

- (ii) a nucleotide or nucleotide analog having the formula



wherein

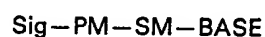
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

fixing the chromosomes from or in said cell;

contacting said fixed chromosomes under hybridizing conditions with said set of clones or DNA fragments or oligo- or polynucleotides, permitting specific hybridization of said set of clones or DNA fragments or oligo- or polynucleotides to said locus or loci in said chromosome of interest;

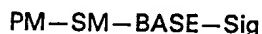
detecting radioactively any signal generated by each of said clones or DNA fragments or oligo- or polynucleotides which have specifically hybridized to said locus or loci in said chromosome of interest, and obtaining a pattern of hybridizations between said set of clones or DNA fragments or oligo- or polynucleotides and said chromosomes; and

identifying said chromosome of interest by means of said hybridization pattern obtained. --

-- 1709. (NEW) A process for identifying a plurality or all of the chromosomes in a cell of interest, the process comprising the steps of:

providing sets of clones or DNA fragments, or oligo- or polynucleotides derived from said clones, wherein each of said set of clones or DNA fragments or oligo- or polynucleotides are specifically hybridizable to a locus or loci in a chromosome of said cell of interest, wherein each of said clones or DNA fragments or oligo- or polynucleotides in said sets are labeled with a different indicator molecule and each of said clones or DNA fragments or oligo- or polynucleotides comprise one or more detectable modified or labeled nucleotides or nucleotide analogs capable of detection, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotide or nucleotide analogs are selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula



wherein

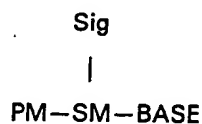
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine, or a pyrimidine analog, at a position other than the C8 position when BASE is a purine or a purine analog, and at a position other than the C7 position when BASE is a 7-deazapurine or a 7-deazapurine analog thereof;

- (ii) a nucleotide or nucleotide analog having the formula



wherein

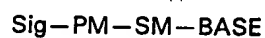
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

fixing the chromosomes from or in said cell;

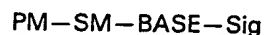
contacting said fixed chromosomes under hybridizing conditions with said sets of clones or DNA fragments or oligo- or polynucleotides, and permitting specific hybridization of said sets of clones or DNA fragments or oligo- or polynucleotides to the locus or loci in said chromosomes; and

detecting radioactively any signal generated by each of said different indicator molecules in said sets of clones or DNA fragments or oligo- or polynucleotides which have specifically hybridized to the locus or loci in said chromosomes, and identifying any one of the chromosomes in said cell of interest. --

-- 1710. (NEW) A process for determining the number of chromosomes in an interphase cell of interest, the process comprising the steps of:

providing sets of clones or DNA fragments, or oligo- or polynucleotides derived from said clones, wherein each of said set of clones or DNA fragments or oligo- or polynucleotides are specifically complementary to or specifically hybridizable with at least one locus or loci in a chromosome of said interphase cell of interest, wherein each of said clones or DNA fragments or oligo- or polynucleotides in said sets comprise one or more detectable modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotide or nucleotide analog are selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula



wherein

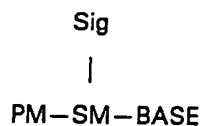
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety or a pyrimidine analog, at a position other than the C8 position when BASE is a purine or a purine analog, and at a position other than the C7 position when BASE is a 7-deazapurine or a 7-deazapurine analog;

- (ii) a nucleotide or nucleotide analog having the formula



wherein

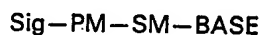
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog, said nucleotide having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of providing a detectable radioactive signal, wherein PM is covalently attached to the SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

contacting said interphase cell under hybridizing conditions with said sets of clones or DNA fragments or oligo- or polynucleotides, and permitting specific hybridization of said sets of clones or DNA fragments or oligo- or polynucleotides to any of the locus or loci in said chromosomes;

detecting radioactively any signals generated by each of said sets of clones or DNA fragments or oligo- or polynucleotides specifically hybridized to the locus or loci in said chromosomes, to obtain a pattern of generated signals; and comparing each generated signal with other generate signals in said pattern, and determining the number of chromosomes in said interphase cell of interest. --

-- 1711. (NEW) A process for preparing a labeled oligo- or polynucleotide of interest, comprising the steps of:

(A) providing either:

(1) one or more detectable chemically modified nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA or an oligo- or polynucleotide of interest, alone or in conjunction with one or more other modified or unmodified nucleic acids selected from the group consisting of nucleotides, oligonucleotides and polynucleotides, wherein said other modified or unmodified nucleic acids are capable of incorporating into an oligo- or polynucleotide of interest, and wherein said chemically modified nucleotides or nucleotide analogs comprise one or more signaling moieties comprising a chelating compound or chelating component capable of providing a detectable radioactive signal, or

(2) an oligo- or polynucleotide of interest comprising one or more of said detectable chemically modified nucleotides or nucleotide analogs, alone or in conjunction with one or more other modified or unmodified nucleic acids selected from the group consisting of nucleotides, oligonucleotides and polynucleotides,

wherein said chemically modified nucleotides or nucleotide analogs are modified on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate moiety, the base moiety or the base analog, and are selected from the group consisting of:

(i)

PM—SM—BASE—Sig

wherein

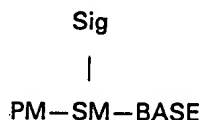
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of providing a detectable radioactive signal, and wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof, and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

(ii)



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of providing a radioactive signal, and wherein said PM is covalently attached to SM, said BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii)



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of providing a detectable radioactive signal; and wherein PM is

covalently attached to SM, BASE is covalently attached SM, and Sig is covalently attached to PM directly or through a linkage group; and said oligo- or polynucleotide of interest; and

(B) either incorporating said one or more modified nucleotides or nucleotide analogs (A)(1) into said oligo- or polynucleotide, and preparing a labeled oligo- or polynucleotide of interest, or preparing said oligo- or polynucleotide of interest from said oligo- or polynucleotide recited in step (A)(2) above. --

-- 1712. (NEW) A process for detecting the presence of a nucleic acid of interest in a sample, comprising the steps of:

providing or generating (i) one or more detectable oligonucleotides or polynucleotides, each of said detectable oligonucleotides or polynucleotides comprising a sequence sufficiently complementary to said nucleic acid of interest or to a portion thereof to hybridize thereto, wherein said one or more detectable oligonucleotides or polynucleotides comprise one or more modified or labeled nucleotides or nucleotide analogues, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety, or the base analog thereof, and (ii) a sample that may contain said nucleic acid of interest;

forming in liquid phase hybrids comprising said one or more detectable oligonucleotides or polynucleotides and said nucleic acid of interest;

separating or resolving in a gel said formed hybrids; and

detecting non-radioactively the separated or resolved hybrids. --

-- 1713. (NEW) The process according to claim 1712, wherein after said hybrid forming step, the liquid phase is subjected to nuclease treatment. --

-- 1714. (NEW) The process according to claim 1712, wherein said nucleic acid of interest is selected from the group consisting of DNA, RNA and DNA-RNA. --

-- 1715. (NEW) The process according to claim 1712, wherein said one or more detectable oligonucleotides or polynucleotides are selected from the group consisting of DNA, RNA and DNA-RNA. --

- 1716. (NEW) The process according to claim 1712, wherein said one or more detectable oligonucleotides or polynucleotides comprise a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --
- 1717. (NEW) The process according to claim 1712, wherein said non-radioactive detection step is carried out directly or indirectly. --
1718. (Wholly Rewritten) The process according to claim 1712, wherein said detecting step is carried out by means of a member selected from the group consisting of enzymatic measurement, a fluorescent measurement, a phosphorescent measurement, a chemiluminescent measurement, a microscopic measurement and an electron density measurement.
- 1719. (NEW) The process according to claim 569, wherein said nucleic acid of interest is selected from the group consisting of DNA, RNA and DNA-RNA. --
- 1720. (NEW) The process according to claim 721, wherein said nucleic acid of interest is selected from the group consisting of DNA, RNA and DNA-RNA. --
- 1721. (NEW) The process according to claim 873, wherein said nucleic acid of interest is selected from the group consisting of DNA, RNA and DNA-RNA. --
- 1722. (NEW) The process according to claim 1025, wherein said nucleic acid of interest is selected from the group consisting of DNA, RNA and DNA-RNA. --
- 1723. (NEW) The process according to any of claims 710, 862, 1014 or 1166, wherein said direct detection is carried out with the same indicator molecules. --
- 1724. (NEW) The process according to any of claims 710, 862, 1014 or 1166, wherein said direct detection is carried out with different indicator molecules. --
- 1725. (NEW) The process according to claim 1400, wherein said direction detection is carried out with the same indicator molecules. --

-- 1726. (NEW) The process according to claim 1400, wherein said direction detection is carried out with different indicator molecules. --

-- 1727. (NEW) The process according to claim 1712, wherein said detecting step comprises localizing said separated or resolved hybrids. --

* * * * *

569. (Twice Amended) A process for determining the sequence of a nucleic acid of interest, comprising the steps of:

providing or generating detectable non-radioactively labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactively modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said one or more detectable non-radioactively modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety, or the base analog thereof;

subjecting said detectable non-radioactively labeled fragments to a sequencing gel to separate or resolve said fragments; and

detecting non-radioactively the presence of each of said separated or resolved fragments by means of said detectable non-radioactively modified or labeled nucleotides or nucleotide analogs, and determining the sequence of said nucleic acid of interest.

-- 570. (NEW) The process according to claim 569, wherein the nucleic acid sequence of interest is derived from an organism. --

-- 571. (NEW) The process according to claim 570, wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing. --

-- 572. (NEW) The process according to claim 571, wherein said organism comprises a mammal. --

-- 573. (NEW) The process according to claim 572, wherein said mammal comprises a human being. --

-- 574. (NEW) The process according to claim 570, wherein said organism is living. --

-- 575. (NEW) The process according to claims 570 or 574, wherein said organism is selected from the group consisting of prokaryotes and eukaryotes. --

-- 576. (NEW) The process according to claim 575, wherein said organism comprises a eukaryote. --

-- 577. (NEW) The process according to claim 576, wherein said eukaryotic nucleic acid sequence of interest is contained within a chromosome. --

-- 578. (NEW) The process according to claim 576, wherein said eukaryote comprises a mammal. --

-- 579. (NEW) The process according to claim 578, wherein said mammalian nucleic acid sequence of interest is contained within a chromosome. --

-- 580. (NEW) The process according to claim 578, wherein said mammal comprises a human being. --

-- 581. (NEW) The process according to claim 580, wherein said human nucleic acid sequence of interest is contained within a chromosome. --

-- 582. (NEW) The process according to claim 581, wherein said human chromosomal nucleic acid sequence of interest is part of a human gene library. --

-- 583. (NEW) The process according to claim 569, wherein said providing or generating step is carried out by means of one or more primers or nucleoside triphosphates or analogs thereof. --

-- 584. (NEW) The process according to claim 583, wherein said nucleoside triphosphates are selected from the group consisting of ribonucleoside triphosphates, deoxyribonucleoside triphosphates, dideoxyribonucleoside triphosphates, and analogs of any of the foregoing. --

-- 585. (NEW) The process according to claim 569, wherein said fragments have been obtained or generated by a nucleic acid sequencing step or technique. --

586. (Twice Amended) The process according to claim 569, wherein the detectable non-radioactively labeled complementary nucleic acid is fragmented prior to separation in said sequencing gel.

587. (Amended) The process according to claim 569, wherein said providing or generating step, the one or more non-radioactively modified or labeled nucleotides or nucleotide analogs have been incorporated into said nucleic acid fragment or fragments.

588. (Amended) The process according to claim 587, wherein at least one of said non-radioactively modified or labeled nucleotides or nucleotide analogs is at a terminus of said fragment or fragments.

-- 589. (NEW) The process according to claim 588, wherein said terminus comprises the 5' or the 3' terminus. --

-- 590. (NEW) The process according to claim 587, wherein said incorporation has been carried out in the presence of a primer. --

-- 591. (NEW) The process according to claim 569, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme. --

-- 592. (NEW) The process according to claim 591, wherein said enzyme comprises terminal transferase. --

-- 593. (NEW) The process according to claim 569, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling. --

594. (Wholly Rewritten) The process according to claim 593, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.

-- 595. (NEW) The process according to claim 593, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase. --

-- 596. (NEW) The process according to claim 569, wherein said incorporation comprises nick translation. --

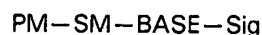
-- 597. (NEW) The process according to claim 569 or 596, wherein said incorporation is carried out by means of a polymerizing enzyme. --

-- 598. (NEW) The process according to claim 597, wherein said polymerizing enzyme comprises a polymerase. --

-- 599. (NEW) The process according to claim 598, wherein said polymerase is selected from the group consisting of DNA polymerase and RNA polymerase. --

600. (Amended) The process according to claim 569, wherein said providing or generating step, the non-radioactively modified or labeled nucleotides or nucleotide analogs comprise one or more members selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

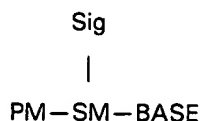
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety or a base analog of any of the foregoing; and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

- (ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

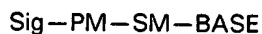
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety, and

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
 Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog, said nucleotide having the formula



wherein

PM is a phosphate moiety or phosphate analog,

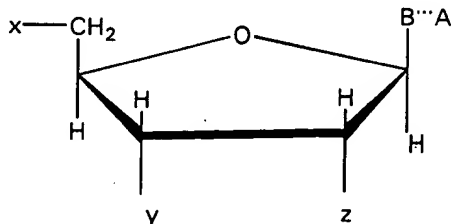
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
 Sig is covalently attached to PM directly or through a linkage group.

601. (Amended) The process according to claim 569, wherein said providing or
 generating step, the non-radioactively modified or labeled nucleotides or nucleotide
 analogs have the structure:



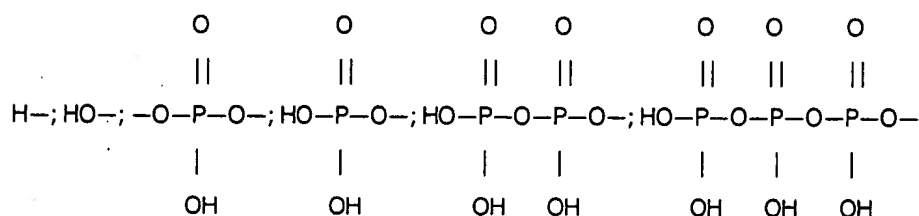
wherein B represents a purine moiety, a 7-deazapurine moiety, a pyrimidine
 moiety, or an analog of any of the foregoing, and B is covalently bonded to the C1'

position of the sugar moiety or sugar analog, provided that whenever B is a purine, a purine analog, a 7-deazapurine moiety or a 7-deazapurine analog, the sugar moiety or sugar analog is attached at the N9 position of the purine moiety, the purine analog, the 7-deazapurine moiety or the 7-deazapurine analog thereof, and whenever B is a pyrimidine moiety or a pyrimidine analog, the sugar moiety or sugar analog is attached at the N1 position of the pyrimidine moiety or the pyrimidine analog;

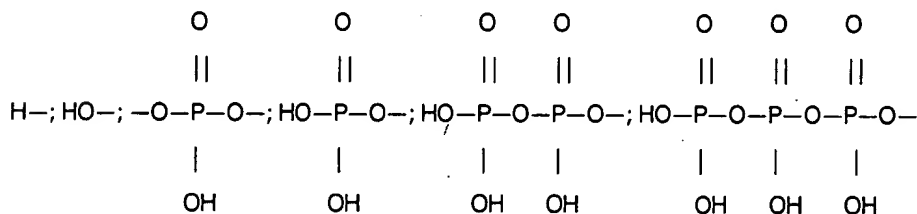
wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal; and

wherein B and A are covalently attached directly or through a linkage group, wherein if B is a purine or a purine analog, A is attached to the 8-position of the purine or purine analog, if B is a 7-deazapurine or 7-deazapurine analog, A is attached to the 7-position of the deazapurine or deazapurine analog, and if B is a pyrimidine or a pyrimidine analog, A is attached to the 5-position of the pyrimidine or pyrimidine analog; and

wherein x comprises a member selected from the group consisting of:



wherein y comprises a member selected from the group consisting of:



wherein z comprises a member selected from the group consisting of H- and HO-.

602. (Amended) The process according to claim 601, wherein y and z [comprise] are H-.

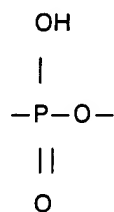
- 603. (NEW) The process according to claim 569, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a mono-phosphate, a di-phosphate, a tri-phosphate and a tetra-phosphate. --
- 604. (NEW) The process according to claim 600, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise a nucleoside mono-, di- or tri-phosphate. --
- 605. (NEW) The process according to claims 569 or 600, wherein said sugar moiety or sugar analog comprises a monosaccharide. --
- 606. (NEW) The process according to claim 605, wherein said monosaccharide comprises a furanose. --
- 607. (NEW) The process according to claim 606, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose. --
- 608. (NEW) The process according to claim 600, wherein said base moiety or base analog BASE in any of said nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --
- 609. (NEW) The process according to claim 600, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --
- 610. (NEW) The process according to claim 600, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to BASE at a position when BASE is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof. --

-- 611. (NEW) The process according to claim 600, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position selected from the group consisting of the N⁴ position when said pyrimidine comprises cytosine, the N² position when said purine comprises adenine or deazaadenine, the N⁶ position when said purine comprises guanine or deazaguanine, and combinations thereof. --

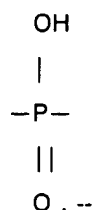
-- 612. (NEW) The process according to claim 606, wherein in said nucleotide (ii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 613. (NEW) The process according to claim 606, wherein in said nucleotide (iii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 614 (NEW) The process according to claim 600, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



and



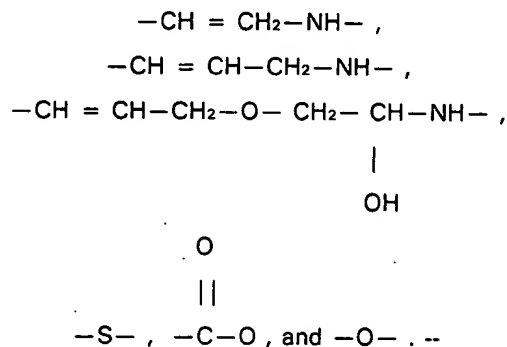
-- 615. (NEW) The process according to claim 600, wherein PM is a mono-, di- or tri-phosphate, and wherein in said nucleotide or nucleotide analog (iii), the Sig moiety is covalently attached to PM through a phosphorus or phosphate oxygen. --

-- 616. (NEW) The process according to claim 600, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal. --

-- 617. (NEW) The process according to claim 600, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $\text{--CH}_2\text{NH--}$ moiety, or both. --

-- 618. (NEW) The process according to claim 600, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group. --

-- 619. (NEW) The process according to claim 600, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



-- 620. (NEW) The process according to claim 600, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety. --

-- 621. (NEW) The process according to claim 600, wherein in any of said nucleotides or nucleotide analogs (i), (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group. --

-- 622. (NEW) The process according to claim 621, wherein said linkage group contains an amine. --

-- 623. (NEW) The process according to claim 622, wherein said amine comprises a primary amine. --

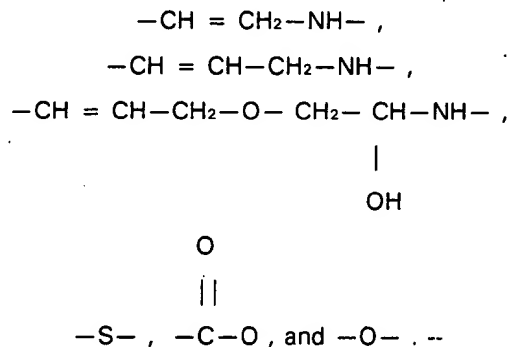
624. (Amended) The process according to claim 621, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

-- 625. (NEW) The process according to claim 601, wherein said covalent attachment does not interfere substantially with the characteristic ability of A to form a detectable non-radioactive signal. --

-- 626. (NEW) The process according to claim 601, wherein said covalent attachment comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $-\text{CH}_2\text{NH}-$ moiety, or both. --

--627. (NEW) The process according to claim 601, wherein said covalent attachment comprises an allylamine group. --

-- 628. (NEW) The process according to claim 601, wherein said covalent attachment comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



-- 629. (NEW) The process according to claim 601, wherein said covalent attachment includes a glycosidic linkage moiety. --

-- 630. (NEW) The process according to claim 601, wherein said A is covalently attached to B through a linkage group. --

-- 631. (NEW) The process according to claim 630, wherein said linkage group contains an amine. --

-- 632. (NEW) The process according to claim 631, wherein said amine comprises a primary amine. --

-- 633. (NEW) The process according to claim 630, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal. --

-- 634. (NEW) The process according to claim 600, wherein Sig comprises at least three carbon atoms. --

-- 635. (NEW) The process according to claim 600, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --

-- 636. (NEW) The process according to claim 600, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms. --

-- 637. (NEW) The process according to claim 600, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic moiety comprising at least five carbon atoms. --

-- 638. (NEW) The process according to claim 637, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent. --

-- 639. (NEW) The process according to claim 600, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --

-- 640. (NEW) The process according to claim 639, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent. --

-- 641. (NEW) The process according to claim 600, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide. --

-- 642. (NEW) The process according to claim 600, wherein Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --

-- 643. (NEW) The process according to claim 642, wherein Sig comprises an electron dense component. --

-- 644. (NEW) The process according to claim 643, wherein said electron dense component comprises ferritin. --

-- 645. (NEW) The process according to claim 642, wherein Sig comprises a magnetic component. --

-- 646. (NEW) The process according to claim 645, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --

-- 647. (NEW) The process according to claim 645, wherein said magnetic component comprises magnetic beads. --

-- 648. (NEW) The process according to claim 600, wherein Sig comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein. --

-- 649. (NEW) The process according to claim 648, wherein the binding protein comprises a lectin. --

-- 650. (NEW) The process according to claim 649, wherein the lectin comprises concanavalin A. --

-- 651. (NEW) The process according to claim 649, wherein said lectin is conjugated to ferritin. --

-- 652. (NEW) The process according to claim 642, wherein Sig comprises an enzyme. --

-- 653. (NEW) The process according to claim 652, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, β -galactosidase, ribonuclease, glucose oxidase, peroxidase, and a combination thereof. --

-- 654. (NEW) The process according to claim 642, wherein Sig comprises a hormone. --

- 655. (NEW) The process according to claim 642, wherein Sig comprises a metal-containing component. --
- 656. (NEW) The process according to claim 655, wherein said metal-containing component is catalytic. --
- 657. (NEW) The process according to claim 600, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule. --
- 658. (NEW) The process according to claim 657, wherein said indicator molecule comprises an aromatic compound. --
- 659. (NEW) The process according to claim 658, wherein said aromatic compound is heterocyclic. --
- 660. (NEW) The process according to claim 659, wherein said heterocyclic aromatic compound is fluorescent. --
- 661. (NEW) The process according to claim 660, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing. --
- 662. (NEW) The process according to claim 661, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --
- 663. (NEW) The process according to claim 642, wherein Sig comprises a fluorescent component. --
- 664. (NEW) The process according to claim 663, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --
- 665. (NEW) The process according to claim 664, wherein said fluorescent component comprises fluorescein. --

-- 666. (NEW) The process according to claim 642, wherein Sig comprises a chemiluminescent component. --

-- 667. (NEW) The process according to claim 642, wherein Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component. --

-- 668. (NEW) The process according to claim 642, wherein Sig comprises an antibody component. --

-- 669. (NEW) The process according to claim 642, wherein Sig comprises a chelating component. --

-- 670. (NEW) The process according to claim 657, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing. --

-- 671. (NEW) The process according to claim 601, wherein A comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --

-- 672. (NEW) The process according to claim 601, wherein A comprises an aliphatic chemical moiety comprising at least four carbon atoms. --

-- 673. (NEW) The process according to claim 601, wherein A comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms. --

-- 674. (NEW) The process according to claim 673, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent. --

-- 675. (NEW) The process according to claim 601, wherein A comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --

-- 676. (NEW) The process according to claim 675, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent. --

- 677. (NEW) The process according to claim 601, wherein A comprises a monosaccharide, polysaccharide or an oligosaccharide. --
- 678. (NEW) The process according to claim 601, wherein A comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --
- 679. (NEW) The process according to claim 678, wherein A comprises an electron dense component. --
- 680. (NEW) The process according to claim 679, wherein said electron dense component comprises ferritin. --
- 681. (NEW) The process according to claim 680, wherein A comprises a magnetic component. --
- 682. (NEW) The process according to claim 681, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --
- 683. (NEW) The process according to claim 681, wherein said magnetic component comprises magnetic beads. --
- 684. (NEW) The process according to claim 601, wherein A comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein. --
- 685. (NEW) The process according to claim 684, wherein the binding protein comprises a lectin. --
- 686. (NEW) The process according to claim 685, wherein the lectin comprises concanavalin A. --

-- 687. (NEW) The process according to claim 685, wherein said lectin is conjugated to ferritin. --

-- 688. (NEW) The process according to claim 678, wherein A comprises an enzyme. --

-- 689. (NEW) The process according to claim 688, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, β -galactosidase, ribonuclease, glucose oxidase, peroxidase, and a combination thereof. --

-- 690. (NEW) The process according to claim 678, wherein A comprises a hormone. --

-- 691. (NEW) The process according to claim 678, wherein A comprises a metal-containing component. --

-- 692. (NEW) The process according to claim 691, wherein said metal-containing component is catalytic. --

-- 693. (NEW) The process according to claim 601, wherein said A comprises an indicator molecule. --

-- 694. (NEW) The process according to claim 693, wherein said indicator molecule comprises an aromatic compound. --

-- 695. (NEW) The process according to claim 694, wherein said aromatic compound is heterocyclic. --

-- 696. (NEW) The process according to claim 695, wherein said heterocyclic aromatic compound is fluorescent. --

-- 697. (NEW) The process according to claim 696, wherein said fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing. --

- 698. (NEW) The process according to claims 696 or 697, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --
- 699. (NEW) The process according to claim 678, wherein A comprises a fluorescent component. --
- 700. (NEW) The process according to claim 699, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --
- 701. (NEW) The process according to claim 700, wherein said fluorescent component comprises fluorescein. --
- 702. (NEW) The process according to claim 678, wherein A comprises a chemiluminescent component. --
- 703. (NEW) The process according to claim 678, wherein A comprises an antigenic or hapten component capable of complexing with an antibody specific to the component. --
- 704. (NEW) The process according to claim 678, wherein A comprises an antibody component. --
- 705. (NEW) The process according to claim 678, wherein A comprises a chelating component. --
- 706. (NEW) The process according to claim 693, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing. --
- 707. (NEW) The process according to claim 569, wherein said labeled nucleic acid fragments are detectable by a non-radioactive means selected from the group consisting of a fluorescent measurement, a chemiluminescent measurement, and a combination thereof. --

-- 708. (NEW) The process according to claim 569, wherein said subjecting step is carried out electrophoretically. --

-- 709. (NEW) The process according to claims 569, 600 or 601, wherein said detecting step is carried out directly. --

-- 710. (NEW) The process according to claim 709, wherein said direct detection is carried out using one or more indicator molecules. --

-- 711. (NEW) The process according to claim 710, wherein said one or more indicator molecules comprise fluoresceinated nucleotides or nucleotide analogs. --

-- 712. (NEW) The process according to claim 711, wherein said fluoresceinated nucleotides or nucleotide analogs comprise fluoresceinated DNA. --

713. (Amended) The process according to claim 709, wherein said detecting step is carried out by means of a directly detectable signal provided by said one or more non-radioactively modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

714. (Amended) The process according to claim 713, wherein in said detecting step the directly detectable signal comprises a member selected from the group consisting of a chelating compound, a fluorogenic compound, [a phosphorescent compound,] a chromogenic compound, a chemiluminescent compound and an electron dense compound.

-- 715. (NEW) The process according to claim 713, wherein in said detecting step the directly detectable signal providing Sig detectable non-radioactive moiety comprises an enzyme. --

716. (Twice Amended) The process according to claims 569, 600 or 601, wherein said detecting step is carried out by means of an indirectly detectable signal provided by said one or more non-radioactively modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

-- 717. (NEW) The process according to claim 716, wherein in said detecting step the indirectly detectable signal is selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme. --

~~DELETED PER 2ND SUPPL. AMEND. 8/31/00 -- 718. (NEW) The process according to claim 717, wherein in said detecting step the indirectly detectable signal is provided by a polynucleotide sequence capable of recognizing a signal containing moiety.~~

719. (Twice Amended) The process according to claim 569, wherein said detectable non-radioactively modified or labeled nucleotides or nucleotide analogs are capable of being detected non-radioactively by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, [a phosphorescent measurement,] a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

720. (Amended) The process according to claim 569, wherein said detecting step comprises localizing said non-radioactively labeled nucleic acid fragments by means of said detectable non-radioactively modified or labeled nucleotides or nucleotide analogs.

721. (Twice Amended) A process for determining the sequence of a nucleic acid of interest, comprising the steps of:

providing or generating detectable non-radioactively labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactively modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said one or more detectable non-radioactively modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety, or the base analog thereof;

introducing or subjecting said detectable non-radioactively labeled fragments to a sequencing gel;

separating or resolving said fragments in said sequencing gel; and

detecting non-radioactively each of the separated or resolved fragments; and determining the sequence of said nucleic acid of interest.

-- 722. (NEW) The process according to claim 721, wherein the nucleic acid sequence of interest is derived from an organism. --

-- 723. (NEW) The process according to claim 722, wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing. --

-- 724. (NEW) The process according to claim 723, wherein said organism comprises a mammal. --

-- 725. (NEW) The process according to claim 724, wherein said mammal comprises a human being. --

-- 726. (NEW) The process according to claim 721, wherein said organism is living. --

-- 727. (NEW) The process according to claims 722 or 726, wherein said organism is selected from the group consisting of prokaryotes and eukaryotes. --

-- 728. (NEW) The process according to claim 727, wherein said organism comprises a eukaryote. --

-- 729. (NEW) The process according to claim 728, wherein said eukaryotic nucleic acid sequence of interest is contained within a chromosome. --

-- 730. (NEW) The process according to claim 728, wherein said eukaryote comprises a mammal. --

-- 731. (NEW) The process according to claim 730, wherein said mammalian nucleic acid sequence of interest is contained within a chromosome. --

-- 732. (NEW) The process according to claim 730, wherein said mammal comprises a human being. --

-- 733. (NEW) The process according to claim 732, wherein said human nucleic acid sequence of interest is contained within a chromosome. --

--734. (NEW) The process according to claim 733, wherein said human chromosomal nucleic acid sequence of interest is part of a human gene library. --

-- 735. (NEW) The process according to claim 721, wherein said providing or generating step is carried out by means of one or more primers or nucleoside triphosphates or analogs thereof. --

-- 736. (NEW) The process according to claim 735, wherein said nucleoside triphosphates are selected from the group consisting of ribonucleoside triphosphates, deoxyribonucleoside triphosphates, dideoxyribonucleoside triphosphates, and analogs of any of the foregoing. --

-- 737. (NEW) The process according to claim 721, wherein said fragments have been obtained or generated by a nucleic acid sequencing step or technique. --

738. (Twice Amended) The process according to claim 721, wherein the detectable non-radioactively labeled complementary nucleic acid is fragmented prior to separation in said sequencing gel.

739. (Amended) The process according to claim 721, wherein said providing or generating step, the one or more non-radioactively modified or labeled nucleotides or nucleotide analogs have been incorporated into said nucleic acid fragment or fragments.

740. (Amended) The process according to claim 739, wherein at least one of said non-radioactively modified or labeled nucleotides or nucleotide analogs is at a terminus of said fragment or fragments.

-- 741. (NEW) The process according to claim 740, wherein said terminus comprises the 5' or the 3' terminus. --

-- 742. (NEW) The process according to claim 739, wherein said incorporation has been carried out in the presence of a primer. --

-- 743. (NEW) The process according to claim 721, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme. --

-- 744. (NEW) The process according to claim 743, wherein said enzyme comprises terminal transferase. --

-- 745. (NEW) The process according to claim 721, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling. --

746. (Wholly Rewritten) The process according to claim 745, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.

-- 747. (NEW) The process according to claim 745, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase. --

-- 748. (NEW) The process according to claim 721, wherein said incorporation comprises nick translation. --

--749. (NEW) The process according to claim 721 or 748, wherein said incorporation is carried out by means of a polymerizing enzyme. --

-- 750. (NEW) The process according to claim 749, wherein said polymerizing enzyme comprises a polymerase. --

-- 751. (NEW) The process according to claim 750, wherein said polymerase is selected from the group consisting of DNA polymerase and RNA polymerase. --

752. (Amended) The process according to claim 721, wherein said providing or generating step, the non-radioactively modified or labeled nucleotides or nucleotide analogs comprise one or more members selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula

PM—SM—BASE—Sig

wherein

PM is a phosphate moiety or phosphate analog,

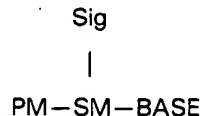
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety
or a base analog of any of the foregoing; and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
Sig is covalently attached to BASE directly or through a linkage group at a position
other than the C5 position when BASE is a pyrimidine moiety or an analog thereof,
at a position other than the C8 position when BASE is a purine moiety or an analog
thereof and at a position other than the C7 position when BASE is a 7-deazapurine
moiety or an analog thereof;

(ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

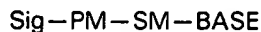
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog, said nucleotide having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

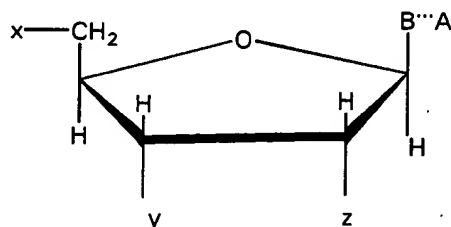
BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
Sig is covalently attached to PM directly or through a linkage group.

753. (Amended) The process according to claim 721, wherein in said providing or
generating step, the non-radioactively modified or labeled nucleotides or nucleotide
analogues have the structure:

(i)



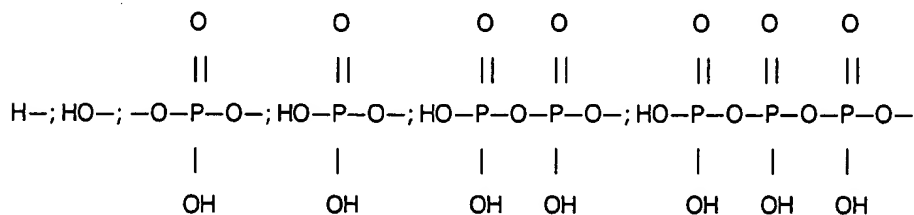
wherein B represents a purine moiety, a 7-deazapurine moiety, a pyrimidine moiety, or an analog of any of the foregoing, and B is covalently bonded to the C1'-position of the sugar moiety or sugar analog, provided that whenever B is a purine, a purine analog, a 7-deazapurine moiety or a 7-deazapurine analog, the sugar moiety or sugar analog is attached at the N9 position of the purine moiety, the purine analog, the 7-deazapurine moiety or the 7-deazapurine analog thereof, and whenever B is a pyrimidine moiety or a pyrimidine analog, the sugar moiety or sugar analog is attached at the N1 position of the pyrimidine moiety or the pyrimidine analog;

wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal; and

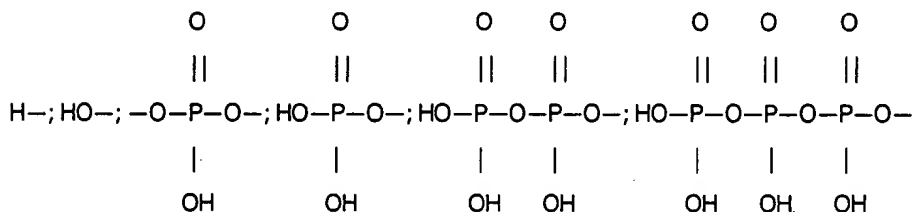
wherein B and A are covalently attached directly or through a linkage group,

wherein if B is a purine or a purine analog, A is attached to the 8-position of the purine or purine analog, if B is a 7-deazapurine or 7-deazapurine analog, A is attached to the 7-position of the deazapurine or deazapurine analog, and if B is a pyrimidine or a pyrimidine analog, A is attached to the 5-position of the pyrimidine or pyrimidine analog; and

wherein x comprises a member selected from the group consisting of:



wherein y comprises a member selected from the group consisting of:



wherein z comprises a member selected from the group consisting of H- and HO-.

754. (Amended) The process according to claim 753, wherein y and z
 [comprise] are [H] H-.

-- 755. (NEW) The process according to claim 721, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a mono-phosphate, a di-phosphate, a tri-phosphate and a tetra-phosphate. --

-- 756. (NEW) The process according to claim 752, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise a nucleoside mono-, di- or tri-phosphate. --

-- 757. (NEW) The process according to claims 721 or 752, wherein said sugar moiety or sugar analog comprises a monosaccharide. --

-- 758. (NEW) The process according to claim 757, wherein said monosaccharide comprises a furanose. --

-- 759. (NEW) The process according to claim 758, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose. --

-- 760. (NEW) The process according to claim 752, wherein said base moiety or base analog BASE in any of said nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --

--761. (NEW) The process according to claim 752, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --

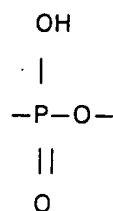
-- 762. (NEW) The process according to claim 752, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to BASE at a position when BASE is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof. --

-- 763. (NEW) The process according to claim 752, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position selected from the group consisting of the N⁴ position when said pyrimidine comprises cytosine, the N² position when said purine comprises adenine or deazaadenine, the N⁶ position when said purine comprises guanine or deazaguanine, and combinations thereof. --

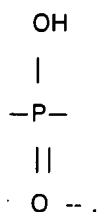
-- 764. (NEW) The process according to claim 758, wherein in said nucleotide (ii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 765. (NEW) The process according to claim 758, wherein in said nucleotide (iii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 766. (NEW) The process according to claim 752, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



and



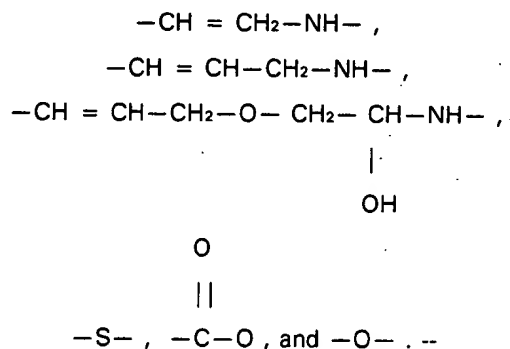
-- 767. (NEW) The process according to claim 752, wherein PM is a mono-, di or tri-phosphate, and wherein said nucleotide or nucleotide analog (iii), the Sig moiety is covalently attached to PM through a phosphorus or phosphate oxygen. --

--768. (NEW) The process according to claim 752, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal. --

-- 769. (NEW) The process according to claim 752, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $\text{--CH}_2\text{NH--}$ moiety, or both. --

-- 770. (NEW) The process according to claim 752, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group. --

-- 771. (NEW) The process according to claim 752, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



-- 772. (NEW) The process according to claim 752, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety. --

--773. (NEW) The process according to claim 752, wherein in any of said nucleotides or nucleotide analogs (i), (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group. --

-- 774. (NEW) The process according to claim 773, wherein said linkage group contains an amine. --

--775. (NEW) The process according to claim 774, wherein said amine comprises a primary amine. --

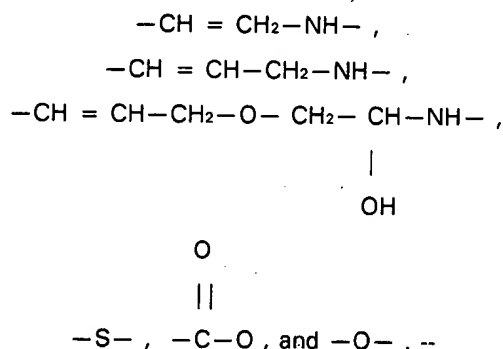
776. (Amended) The process according to claim 773, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

-- 777. (NEW) The process according to claim 753, wherein said covalent attachment does not interfere substantially with the characteristic ability of A to form a detectable non-radioactive signal. --

-- 778. (NEW) The process according to claim 753, wherein said covalent attachment comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $-\text{CH}_2\text{NH}-$ moiety, or both. --

-- 779. (NEW) The process according to claim 753, wherein said covalent attachment comprises an allylamine group. --

--780. (NEW) The process according to claim 753, wherein said covalent attachment comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



-- 781. (NEW) The process according to claim 753, wherein said covalent attachment includes a glycosidic linkage moiety. --

-- 782. (NEW) The process according to claim 753, wherein said A is covalently attached to B through a linkage group. --

-- 783. (NEW) The process according to claim 782, wherein said linkage group contains an amine. --

-- 784. (NEW) The process according to claim 783, wherein said amine comprises a primary amine. --

-- 785. (NEW) The process according to claim 782, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal. --

-- 786. (NEW) The process according to claim 752, wherein Sig comprises at least three carbon atoms. --

-- 787. (NEW) The process according to claim 752, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --

-- 788. (NEW) The process according to claim 752, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms. --

-- 789. (NEW) The process according to claim 752, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic moiety comprising at least five carbon atoms. --

-- 790. (NEW) The process according to claim 789, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent. --

-- 791. (NEW) The process according to claim 752, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --

-- 792. (NEW) The process according to claim 791, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent. --

-- 793. (NEW) The process according to claim 752, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide. --

-- 794. (NEW) The process according to claim 752, wherein Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --

--795. (NEW) The process according to claim 794, wherein Sig comprises an electron dense component. --

-- 796. (NEW) The process according to claim 795, wherein said electron dense component comprises ferritin. --

-- 797. (NEW) The process according to claim 794, wherein Sig comprises a magnetic component. --

-- 798. (NEW) The process according to claim 797, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --

-- 799. (NEW) The process according to claim 797, wherein said magnetic component comprises magnetic beads. --

-- 800. (NEW) The process according to claim 752, wherein Sig comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein. --

-- 801. (NEW) The process according to claim 800, wherein the binding protein comprises a lectin. --

--802. (NEW) The process according to claim 801, wherein the lectin comprises concanavalin A. --

-- 803. (NEW) The process according to claim 801, wherein said lectin is conjugated to ferritin. --

-- 804. (NEW) The process according to claim 794, wherein Sig comprises an enzyme. --

- 805. (NEW) The process according to claim 804, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, β galactosidase, ribonuclease, glucose oxidase, peroxidase, and a combination thereof. --
- 806. (NEW) The process according to claim 794, wherein Sig comprises a hormone. --
- 807. (NEW) The process according to claim 794, wherein Sig comprises a metal-containing component. --
- 808. (NEW) The process according to claim 807, wherein said metal-containing component is catalytic. --
- 809. (NEW) The process according to claim 752, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule. --
- 810. (NEW) The process according to claim 809, wherein said indicator molecule comprises an aromatic compound. --
- 811. (NEW) The process according to claim 810, wherein said aromatic compound is heterocyclic. --
- 812. (NEW) The process according to claim 811, wherein said heterocyclic aromatic compound is fluorescent. --
- 813. (NEW) The process according to claim 812, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing. --
- 814. (NEW) The process according to claim 813, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --
- 815. (NEW) The process according to claim 794, wherein Sig comprises a fluorescent component. --

-- 816. (NEW) The process according to claim 815, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --

-- 817. (NEW) The process according to claim 816, wherein said fluorescent component comprises fluorescein. --

-- 818. (NEW) The process according to claim 794, wherein Sig comprises a chemiluminescent component. --

--819. (NEW) The process according to claim 794, wherein Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component. --

-- 820. (NEW) The process according to claim 794, wherein Sig comprises an antibody component. --

-- 821. (NEW) The process according to claim 794, wherein Sig comprises a chelating component. --

-- 822. (NEW) The process according to claim 809, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing. --

-- 823. (NEW) The process according to claim 753, wherein A comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --

-- 824. (NEW) The process according to claim 753, wherein A comprises an aliphatic chemical moiety comprising at least four carbon atoms. --

-- 825. (NEW) The process according to claim 753, wherein A comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms. --

-- 826. (NEW) The process according to claim 825, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent. --

--827. (NEW) The process according to claim 753, wherein A comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --

--828. (NEW) The process according to claim 827, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent. --

-- 829. (NEW) The process according to claim 753, wherein A comprises a monosaccharide, polysaccharide or an oligosaccharide. --

-- 830. (NEW) The process according to claim 753, wherein A comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --

-- 831. (NEW) The process according to claim 830, wherein A comprises an electron dense component. --

-- 832. (NEW) The process according to claim 831, wherein said electron dense component comprises ferritin. --

-- 833. (NEW) The process according to claim 830, wherein A comprises a magnetic component. --

-- 834. (NEW) The process according to claim 833, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --

-- 835. (NEW) The process according to claim 833, wherein said magnetic component comprises magnetic beads. --

-- 836. (NEW) The process according to claim 753, wherein A comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein. --

- 837. (NEW) The process according to claim 836, wherein the binding protein comprises a lectin. --
- 838. (NEW) The process according to claim 837, wherein the lectin comprises concanavalin A. --
- 839. (NEW) The process according to claim 837, wherein said lectin is conjugated to ferritin. --
- 840. (NEW) The process according to claim 830, wherein A comprises an enzyme. --
- 841. (NEW) The process according to claim 840, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, β -galactosidase, ribonuclease, glucose oxidase, peroxidase, and a combination thereof. --
- 842. (NEW) The process according to claim 830, wherein A comprises a hormone. --
- 843. (NEW) The process according to claim 830, wherein A comprises a metal-containing component. --
- 844. (NEW) The process according to claim 843, wherein said metal-containing component is catalytic. --
- 845. (NEW) The process according to claim 753, wherein said A comprises an indicator molecule. --
- 846. (NEW) The process according to claim 845, wherein said indicator molecule comprises an aromatic compound. --
- 847. (NEW) The process according to claim 846, wherein said aromatic compound is heterocyclic. --

- 848. (NEW) The process according to claim 847, wherein said heterocyclic aromatic compound is fluorescent. --
- 849. (NEW) The process according to claim 848, wherein said fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing. --
- 850. (NEW) The process according to claims 848 or 849, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --
- 851. (NEW) The process according to claim 830, wherein A comprises a fluorescent component. --
- 852. (NEW) The process according to claim 851, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --
- 853. (NEW) The process according to claim 852, wherein said fluorescent component comprises fluorescein. --
- 854. (NEW) The process according to claim 830, wherein A comprises a chemiluminescent component. --
- 855. (NEW) The process according to claim 830, wherein A comprises an antigenic or hapten component capable of complexing with an antibody specific to the component. --
- 856. (NEW) The process according to claim 830, wherein A comprises an antibody component. --
- 857. (NEW) The process according to claim 830, wherein A comprises a chelating component. --

-- 858. (NEW) The process according to claim 845, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing. --

859. (Twice Amended) The process according to claim 721, wherein said detectable non-radioactively labeled nucleic acid fragments are detectable by a non-radioactive means selected from the group consisting of a fluorescent measurement, a chemiluminescent measurement, and a combination thereof.

-- 860. (NEW) The process according to claim 721, wherein said separating or resolving step is carried out electrophoretically. --

-- 861. (NEW) The process according to claims 721, 752 or 753, wherein said detecting step is carried out directly. --

-- 862. (NEW) The process according to claim 861, wherein said direct detection is carried out using one or more indicator molecules. --

-- 863. (NEW) The process according to claim 862, wherein said one or more indicator molecules comprise fluoresceinated nucleotides or nucleotide analogs. --

-- 864. (NEW) The process according to claim 863, wherein said fluoresceinated nucleotides or nucleotide analogs comprise fluoresceinated DNA. --

-- 865. (NEW) The process according to claim 861, wherein said detecting step is carried out by means of a directly detectable signal provided by said one or more modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety. --

866. (Amended) The process according to claim 865, wherein in said detecting step the directly detectable signal comprises a member selected from the group consisting of a chelating compound, a fluorogenic compound, [a phosphorescent compound,] a chromogenic compound, a chemiluminescent compound and an electron dense compound.

-- 867. (NEW) The process according to claim 865, wherein in said detecting step the directly detectable signal providing Sig detectable non-radioactive moiety comprises an enzyme. --

868. (Amended) The process according to claims 721, 752 or 753, wherein said detecting step is carried out by means of a indirectly detectable signal provided by said one or more non-radioactively modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

-- 869. (NEW) The process according to claim 868, wherein in said detecting step the indirectly detectable signal is selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme. --

~~DELETED PER 2ND SUPPL. AMEND. 8/31/00 -- 870. (NEW) The process according to claim 868, wherein in said detecting step the indirectly detectable signal is provided by a polynucleotide sequence capable of recognizing a signal containing moiety. --~~

871. (Twice Amended) The process according to claim 721, wherein said one or more modified or labeled nucleotides or nucleotide analogs are capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, [a phosphorescent measurement,] a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

872. (Twice Amended) The process according to claim 721, wherein said detecting step comprises localizing said detectable non-radioactive labeled nucleic acid fragments by means of said one or more non-radioactive modified or labeled nucleotides or nucleotide analogs.

873. (Twice Amended) A process for determining the sequence of a nucleic acid of interest, comprising the steps of:

providing or generating detectable non-radioactive labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety or the base analog thereof;

detecting non-radioactively the detectable non-radioactive labeled nucleic acid fragments with a sequencing gel; and

determining the sequence of said nucleic acid of interest.

-- 874. (NEW) The process according to claim 873, wherein the nucleic acid sequence of interest is derived from an organism. --

-- 875. (NEW) The process according to claim 874, wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing. --

-- 876. (NEW) The process according to claim 875, wherein said organism comprises a mammal. --

-- 877. (NEW) The process according to claim 876, wherein said mammal comprises a human being. --

-- 878. (NEW) The process according to claim 874, wherein said organism is living. --

-- 879. (NEW) The process according to claims 874 or 878, wherein said organism is selected from the group consisting of prokaryotes and eukaryotes. --

-- 880. (NEW) The process according to claim 879, wherein said organism comprises a eukaryote. --

-- 881. (NEW) The process according to claim 880, wherein said eukaryotic nucleic acid sequence of interest is contained within a chromosome. --

-- 882. (NEW) The process according to claim 880, wherein said eukaryote comprises a mammal. --

-- 883. (NEW) The process according to claim 882, wherein said mammalian nucleic acid sequence of interest is contained within a chromosome. --

-- 884. (NEW) The process according to claim 882, wherein said mammal comprises a human being. --

-- 885. (NEW) The process according to claim 884, wherein said human nucleic acid sequence of interest is contained within a chromosome. --

-- 886. (NEW) The process according to claim 885, wherein said human chromosomal nucleic acid sequence of interest is part of a human gene library. --

--887. (NEW) The process according to claim 873, wherein said providing or generating step is carried out by means of one or more primers or nucleoside triphosphates or analogs thereof. --

-- 888. (NEW) The process according to claim 887, wherein said nucleoside triphosphates are selected from the group consisting of ribonucleoside triphosphates, deoxyribonucleoside triphosphates, dideoxyribonucleoside triphosphates, and analogs of any of the foregoing. --

-- 889. (NEW) The process according to claim 873, wherein said fragments have been obtained or generated by a nucleic acid sequencing step or technique. --

890. (Twice Amended) The process according to claim 873, wherein the detectable non-radioactive labeled complementary nucleic acid is fragmented and separated prior to detecting in said sequencing gel.

891. (Amended) The process according to claim 873, wherein in said providing or generating step, the one or more non-radioactive modified or labeled nucleotides or nucleotide analogs have been incorporated into said nucleic acid fragment or fragments.

892. (Amended) The process according to claim 891, wherein at least one of said non-radioactive modified or labeled nucleotides or nucleotide analogs is at a terminus of said fragment or fragments.

-- 893. (NEW) The process according to claim 892, wherein said terminus comprises the 5' or the 3' terminus. --

-- 894. (NEW) The process according to claim 891, wherein said incorporation has been carried out in the presence of a primer. --

-- 895. (NEW) The process according to claim 873, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme. --

-- 896. (NEW) The process according to claim 895, wherein said enzyme comprises terminal transferase. --

-- 897. (NEW) The process according to claim 873, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling. --

898. (Wholly Rewritten) The process according to claim 897, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.

-- 899. (NEW) The process according to claim 898, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase. --

-- 900. (NEW) The process according to claim 873, wherein said incorporation comprises nick translation. --

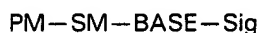
-- 901. (NEW) The process according to claim 873 or 900, wherein said incorporation is carried out by means of a polymerizing enzyme. --

--902. (NEW) The process according to claim 901, wherein said polymerizing enzyme comprises a polymerase. --

-- 903. (NEW) The process according to claim 902, wherein said polymerizing enzyme is selected from the group consisting of DNA polymerase and RNA polymerase. --

904. (Amended) The process according to claim 873, wherein in said providing or generating step, the non-radioactive modified or labeled nucleotides or nucleotide analogs comprise one or more members selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

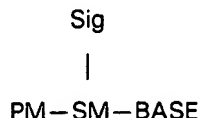
BASE is a pyrimidine, a purine or a 7-deazapurine base moiety

or a base analog of any of the foregoing; and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

- (ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

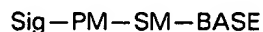
BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and

Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog, said nucleotide having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

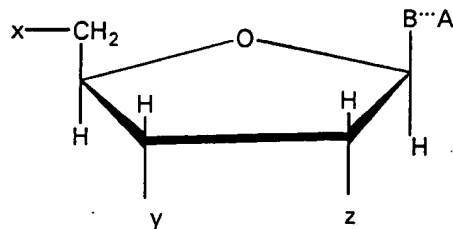
Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and

Sig is covalently attached to PM directly or through a linkage group.

905. (Amended) The process according to claim 873, wherein in said providing or generating step, the non-radioactive modified or labeled nucleotides or nucleotide analogs have the structure:

(i)



wherein B represents a purine moiety, a 7-deazapurine moiety, a pyrimidine moiety or an analog of any of the foregoing, and B is covalently bonded to the C1' position of the sugar moiety or sugar analog, provided that whenever B is a purine, a purine analog, a 7-deazapurine moiety or a 7-deazapurine analog, the sugar moiety or sugar analog is attached at the N9 position of the purine moiety, the purine analog, the 7-deazapurine moiety or the 7-deazapurine analog thereof, and

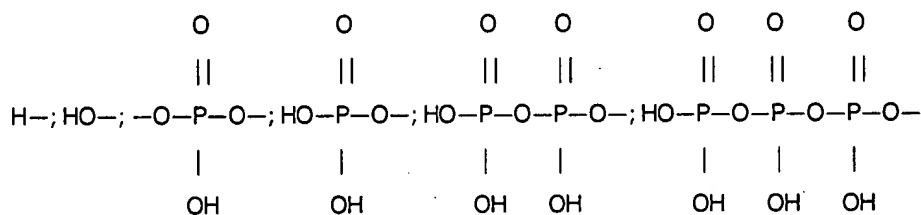
whenever B is a pyrimidine moiety or a pyrimidine analog, the sugar moiety or sugar analog is attached at the N1 position of the pyrimidine moiety or the pyrimidine analog;

wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal; and

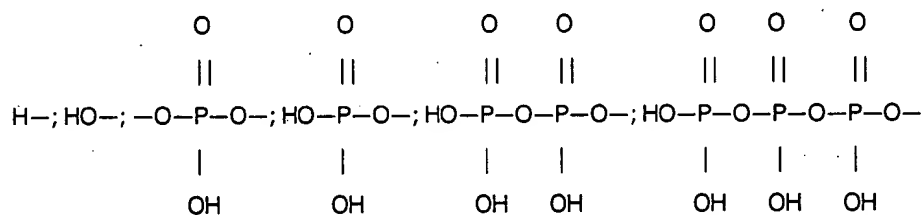
wherein B and A are covalently attached directly or through a linkage group,

wherein if B is a purine or a purine analog, A is attached to the 8-position of the purine or purine analog, if B is a 7-deazapurine or 7-deazapurine analog, A is attached to the 7-position of the deazapurine or deazapurine analog, and if B is a pyrimidine or a pyrimidine analog, A is attached to the 5-position of the pyrimidine or pyrimidine analog; and

wherein x comprises a member selected from the group consisting of:



wherein y comprises a member selected from the group consisting of:



wherein z comprises a member selected from the group consisting of H- and HO-.

906. (Amended) The process according to claim 905, wherein y and z [comprise] are [H] H-.

-- 907. (NEW) The process according to claim 873, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a mono-phosphate, a di-phosphate, a tri-phosphate and a tetra-phosphate. --

-- 908. (NEW) The process according to claim 904, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise a nucleoside mono-, di- or tri-phosphate. --

-- 909. (NEW) The process according to claims 873 or 904, wherein said sugar moiety or sugar analog comprises a monosaccharide. --

-- 910. (NEW) The process according to claim 909, wherein said monosaccharide comprises a furanose. --

-- 911. (NEW) The process according to claim 910, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose. --

-- 912. (NEW) The process according to claim 904, wherein said base moiety or base analog BASE in any of said nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --

-- 913. (NEW) The process according to claim 904, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --

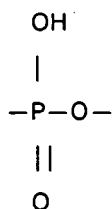
-- 914. (NEW) The process according to claim 904, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to BASE at a position when BASE is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof. --

-- 915. (NEW) The process according to claim 904, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position selected from the group consisting of the N⁴ position when said pyrimidine comprises cytosine, the N² position when said purine comprises adenine or deazaadenine, the N⁶ position when said purine comprises guanine or deazaguanine, and combinations thereof. --

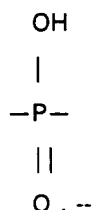
-- 916. (NEW) The process according to claim 910, wherein in said nucleotide (ii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 917. (NEW) The process according to claim 910, wherein in said nucleotide (iii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 918. (NEW) The process according to claim 904, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



and



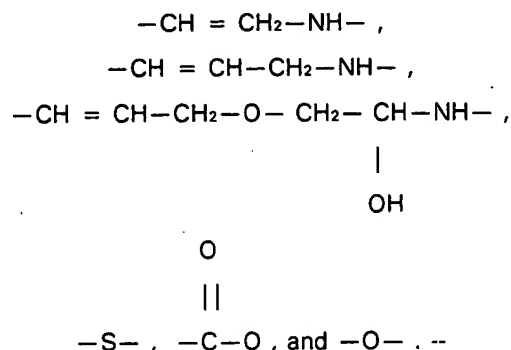
-- 919. (NEW) The process according to claim 904, wherein PM is a mono-, di- or tri-phosphate, and wherein in said nucleotide or nucleotide analog (iii), the Sig moiety is covalently attached to PM through a phosphorus or phosphate oxygen. --

-- 920. (NEW) The process according to claim 904, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal. --

-- 921. (NEW) The process according to claim 904, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $-\text{CH}_2\text{NH}-$ moiety, or both. --

-- 922. (NEW) The process according to claim 904, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group. --

-- 923. (NEW) The process according to claim 904, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



-- 924. (NEW) The process according to claim 904, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety. --

-- 925. (NEW) The process according to claim 904, wherein in any of said nucleotides or nucleotide analogs (i), (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group. --

-- 926. (NEW) The process according to claim 925, wherein said linkage group contains an amine. --

--927. (NEW) The process according to claim 926, wherein said amine comprises a primary amine. --

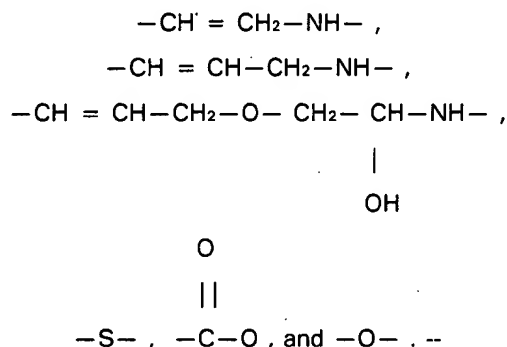
928. (Amended) The process according to claim 925, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

-- 929. (NEW) The process according to claim 905, wherein said covalent attachment does not interfere substantially with the characteristic ability of A to form a detectable non-radioactive signal. --

-- 930. (NEW) The process according to claim 905, wherein said covalent attachment comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $-\text{CH}_2\text{NH}-$ moiety, or both. --

-- 931. (NEW) The process according to claim 905, wherein said covalent attachment comprises an allylamine group. --

-- 932. (NEW) The process according to claim 905, wherein said covalent attachment comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



-- 933. (NEW) The process according to claim 905, wherein said covalent attachment includes a glycosidic linkage moiety. --

-- 934. (NEW) The process according to claim 905, wherein said A is covalently attached to B through a linkage group. --

-- 935. (NEW) The process according to claim 934, wherein said linkage group contains an amine. --

-- 936. (NEW) The process according to claim 935, wherein said amine comprises a primary amine. --

-- 937. (NEW) The process according to claim 934, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal. --

-- 938. (NEW) The process according to claim 904, wherein Sig comprises at least three carbon atoms. --

-- 939. (NEW) The process according to claim 904, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --

-- 940. (NEW) The process according to claim 904, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms. --

-- 941. (NEW) The process according to claim 904, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic moiety comprising at least five carbon atoms. --

-- 942. (NEW) The process according to claim 941, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent. --

-- 943. (NEW) The process according to claim 904, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --

-- 944. (NEW) The process according to claim 943, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent. --

-- 945. (NEW) The process according to claim 904, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide. --

-- 946. (NEW) The process according to claim 904, wherein Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --

-- 947. (NEW) The process according to claim 946, wherein Sig comprises an electron dense component. --

-- 948. (NEW) The process according to claim 947, wherein said electron dense component comprises ferritin. --

-- 949. (NEW) The process according to claim 946, wherein Sig comprises a magnetic component. --

-- 950. (NEW) The process according to claim 949, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --

-- 951. (NEW) The process according to claim 949, wherein said magnetic component comprises magnetic beads. --

-- 952. (NEW) The process according to claim 904, wherein Sig comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein. --

-- 953. (NEW) The process according to claim 952, wherein the binding protein comprises a lectin. --

-- 954. (NEW) The process according to claim 953, wherein the lectin comprises concanavalin A. --

-- 955. (NEW) The process according to claim 953, wherein said lectin is conjugated to ferritin. --

-- 956. (NEW) The process according to claim 946, wherein Sig comprises an enzyme. --

-- 957. (NEW) The process according to claim 956, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, β -galactosidase, ribonuclease, glucose oxidase, peroxidase, and a combination thereof. --

-- 958. (NEW) The process according to claim 946, wherein Sig comprises a hormone. --

-- 959. (NEW) The process according to claim 946, wherein Sig comprises a metal-containing component. --

-- 960. (NEW) The process according to claim 959, wherein said metal-containing component is catalytic. --

-- 961. (NEW) The process according to claim 904, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule. --

-- 962. (NEW) The process according to claim 961, wherein said indicator molecule comprises an aromatic compound. --

-- 963. (NEW) The process according to claim 962, wherein said aromatic compound is heterocyclic. --

-- 964. (NEW) The process according to claim 963, wherein said heterocyclic aromatic compound is fluorescent. --

-- 965. (NEW) The process according to claim 904, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing. --

-- 966. (NEW) The process according to claim 965, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --

-- 967. (NEW) The process according to claim 946, wherein Sig comprises a fluorescent component. --

-- 968. (NEW) The process according to claim 967, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --

- 969. (NEW) The process according to claim 968, wherein said fluorescent component comprises fluorescein. --
- 970. (NEW) The process according to claim 946, wherein Sig comprises a chemiluminescent component. --
- 971. (NEW) The process according to claim 946, wherein Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component. --
- 972. (NEW) The process according to claim 946, wherein Sig comprises an antibody component. --
- 973. (NEW) The process according to claim 946, wherein Sig comprises a chelating component. --
- 974. (NEW) The process according to claim 961, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing. --
- 975. (NEW) The process according to claim 905, wherein A comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --
- 976. (NEW) The process according to claim 905, wherein A comprises an aliphatic chemical moiety comprising at least four carbon atoms. --
- 977. (NEW) The process according to claim 905, wherein A comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms. --
- 978. (NEW) The process according to claim 977, wherein. --
- 979. (NEW) The process according to claim 905, wherein A comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --

-- 980. (NEW) The process according to claim 979, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent. --

-- 981. (NEW) The process according to claim 905, wherein A comprises a monosaccharide, polysaccharide or an oligosaccharide. --

-- 982. (NEW) The process according to claim 905, wherein A comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --

-- 983. (NEW) The process according to claim 982, wherein A comprises an electron dense component. --

-- 984. (NEW) The process according to claim 983, wherein said electron dense component comprises ferritin. --

-- 985. (NEW) The process according to claim 982, wherein A comprises a magnetic component. --

-- 986. (NEW) The process according to claim 985, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --

-- 987. (NEW) The process according to claim 985, wherein said magnetic component comprises magnetic beads. --

-- 988. (NEW) The process according to claim 905, wherein A comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein. --

-- 989. (NEW) The process according to claim 988, wherein the binding protein comprises a lectin. --

-- 990. (NEW) The process according to claim 989, wherein the lectin comprises concanavalin A. --

- 991. (NEW) The process according to claim 989, wherein said lectin is conjugated to ferritin. --
- 992. (NEW) The process according to claim 982, wherein A comprises an enzyme. --
- 993. (NEW) The process according to claim 992, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, β -galactosidase, ribonuclease, glucose oxidase, peroxidase, and a combination thereof. --
- 994. (NEW) The process according to claim 982, wherein A comprises a hormone. --
- 995. (NEW) The process according to claim 982, wherein A comprises a metal-containing component. --
- 996. (NEW) The process according to claim 995, wherein said metal-containing component is catalytic. --
- 997. (NEW) The process according to claim 905, wherein said A comprises an indicator molecule. --
- 998. (NEW) The process according to claim 997, wherein said indicator molecule comprises an aromatic compound. --
- 999. (NEW) The process according to claim 998, wherein said aromatic compound is heterocyclic. --
- 1000. (NEW) The process according to claim 999, wherein said heterocyclic aromatic compound is fluorescent. --
- 1001. (NEW) The process according to claim 1000, wherein said fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing. --

-- 1002. (NEW) The process according to claims 1000 or 1001, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --

-- 1003. (NEW) The process according to claim 982, wherein A comprises a fluorescent component. --

-- 1004. (NEW) The process according to claim 1003, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --

-- 1005. (NEW) The process according to claim 1004, wherein said fluorescent component comprises fluorescein. --

--1006. (NEW) The process according to claim 982, wherein A comprises a chemiluminescent component. --

-- 1007. (NEW) The process according to claim 982, wherein A comprises an antigenic or hapten component capable of completing with an antibody specific to the component. --

-- 1008. (NEW) The process according to claim 982, wherein A comprises an antibody component. --

-- 1009. (NEW) The process according to claim 982, wherein A comprises a chelating component. --

-- 1010. (NEW) The process according to claim 1009, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing. --

1011. (Twice Amended) The process according to claim 873, wherein said detectable non-radioactive labeled nucleic acid fragments are detectable by a non-radioactive means selected from the group consisting of a fluorescent measurement, a chemiluminescent measurement, and a combination thereof.

1012. (Twice Amended) The process according to claim 873, wherein said detecting step, the detectable non-radioactive labeled nucleic acid fragments are separated or resolved electrophoretically.

-- 1013. (NEW) The process according to claims 873, 904 or 905, wherein said detecting step is carried out directly. --

--1014. (NEW) The process according to claim 1013, wherein said direct detection is carried out using one or more indicator molecules. --

-- 1015. (NEW) The process according to claim 1014, wherein said one or more indicator molecules comprise fluoresceinated nucleotides or nucleotide analogs. --

-- 1016. (NEW) The process according to claim 1015, wherein said fluoresceinated nucleotides or nucleotide analogs comprise fluoresceinated DNA. --

1017. (Amended) The process according to claim 1016, wherein said detecting step is carried out by means of a directly detectable signal provided by said one or more non-radioactive modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

1018. (Amended) The process according to claim 1013, wherein said detecting step the directly detectable signal comprises a member selected from the group consisting of a chelating compound, a fluorogenic compound, [a phosphorescent compound,] a chromogenic compound, a chemiluminescent compound and an electron dense compound.

-- 1019. (NEW) The process according to claim 1013, wherein said detecting step the directly detectable signal providing Sig detectable non-radioactive moiety comprises an enzyme. --

1020. (Amended) The process according to claims 873, 904 or 905, wherein said detecting step is carried out by means of an indirectly detectable signal provided by said one or more non-radioactive modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

-- 1021. (NEW) The process according to claim 1020, wherein said detecting step the indirectly detectable signal is selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme. --

~~DELETED PER 2ND SUPPL. AMEND. 8/31/00 -- 1022. (NEW) The process according to claim 1020, wherein said detecting step the indirectly detectable signal is provided by a polynucleotide sequence capable of recognizing a signal containing moiety. --~~

1023. (Twice Amended) The process according to claim 873, wherein said one or more non-radioactive modified or labeled nucleotides or nucleotide analogs are capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, [a phosphorescent measurement,] a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

1024. (Twice Amended) The process according to claim 873, wherein said detecting step comprises localizing said detectable non-radioactive labeled nucleic acid fragments by means of said one or more non-radioactive modified or labeled nucleotides or nucleotide analogs.

1025. (Twice Amended) A process for determining the sequence of a nucleic acid of interest, comprising the step of detecting non-radioactively with a sequencing gel one or more detectable non-radioactive labeled nucleic acid fragments comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs have been modified on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the base moiety or the base analog thereof.

-- 1026. (NEW) The process according to claim 1025, wherein the nucleic acid sequence of interest is derived from an organism. --

-- 1027. (NEW) The process according to claim 1026, wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing. --

-- 1028. (NEW) The process according to claim 1027, wherein said organism comprises a mammal. --

-- 1029. (NEW) The process according to claim 1028, wherein said mammal comprises a human being. --

-- 1030. (NEW) The process according to claim 1026, wherein said organism is living. --

-- 1031. (NEW) The process according to claims 1026 or 1030, wherein said organism is selected from the group consisting of prokaryotes and eukaryotes. --

-- 1032. (NEW) The process according to claim 1031, wherein said organism comprises a eukaryote. --

-- 1033. (NEW) The process according to claim 1032, wherein said eukaryotic nucleic acid sequence of interest is contained within a chromosome. --

--1034. (NEW) The process according to claim 1032, wherein said eukaryote comprises a mammal. --

--1035. (NEW) The process according to claim 1034, wherein said mammalian nucleic acid sequence of interest is contained within a chromosome. --

-- 1036. (NEW) The process according to claim 1034, wherein said mammal comprises a human being. --

-- 1037. (NEW) The process according to claim 1036, wherein said human nucleic acid sequence of interest is contained within a chromosome. --

-- 1038. (NEW) The process according to claim 1037, wherein said human chromosomal nucleic acid sequence of interest is part of a human gene library. --

-- 1039. (NEW) The process according to claim 1025, wherein said providing or generating step is carried out by means of one or more primers or nucleoside triphosphates or analogs thereof. --

-- 1040. (NEW) The process according to claim 1039, wherein said nucleoside triphosphates are selected from the group consisting of ribonucleoside triphosphates, deoxyribonucleoside triphosphates, dideoxyribonucleoside triphosphates, and analogs of any of the foregoing. --

-- 1041. (NEW) The process according to claim 1025, wherein said fragments have been obtained or generated by a nucleic acid sequencing step or technique. --

1042. (Twice Amended) The process according to claim 1025, wherein the detectable non-radioactive labeled complementary nucleic acid is fragmented prior to separation in said sequencing gel.

1043. (Amended) The process according to claim 1025, wherein said providing or generating step, the one or more non-radioactive modified or labeled nucleotides or nucleotide analogs have been incorporated into said nucleic acid fragment or fragments.

1044. (Amended) The process according to claim 1043, wherein at least one of said non-radioactive modified or labeled nucleotides or nucleotide analogs is at a terminus of said fragment or fragments.

-- 1045. (NEW) The process according to claim 1044, wherein said terminus comprises the 5' or the 3' terminus. --

-- 1046. (NEW) The process according to claim 1043, wherein said incorporation has been carried out in the presence of a primer. --

-- 1047. (NEW) The process according to claim 1025, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme. --

-- 1048. (NEW) The process according to claim 1047, wherein said enzyme comprises terminal transferase. --

-- 1049. (NEW) The process according to claim 1025, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling. --

1050. (Wholly Rewritten) The process according to claim 1049, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.

-- 1051. (NEW) The process according to claim 1049, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase. --

-- 1052. (NEW) The process according to claim 1025, wherein said incorporation comprises nick translation. --

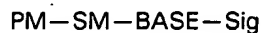
-- 1053. (NEW) The process according to claim 1025 or 1052, wherein said incorporation is carried out by means of a polymerizing enzyme. --

-- 1054. (NEW) The process according to claim 1053, wherein said polymerizing enzyme comprises a polymerase. --

-- 1055. (NEW) The process according to claim 1054, wherein said polymerase is selected from the group consisting of DNA polymerase and RNA polymerase. --

1056. (Amended) The process according to claim 1025, wherein said providing or generating step, the non-radioactive modified or labeled nucleotides or nucleotide analogs comprise one or more members selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

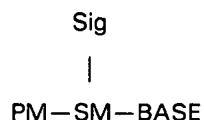
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety
or a base analog of any of the foregoing; and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
Sig is covalently attached to BASE directly or through a linkage group at a position
other than the C5 position when BASE is a pyrimidine moiety or an analog thereof,
at a position other than the C8 position when BASE is a purine moiety or an analog
thereof and at a position other than the C7 position when BASE is a 7-deazapurine
moiety or an analog thereof;

(ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

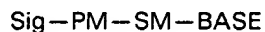
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog, said nucleotide having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

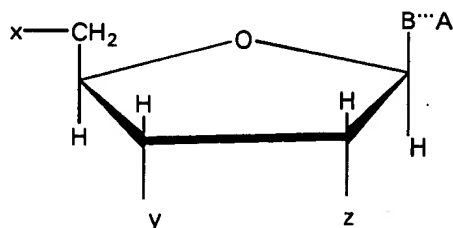
BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
Sig is covalently attached to PM directly or through a linkage group.

1057. (Amended) The process according to claim 1025, wherein said providing or generating step, the non-radioactive modified or labeled nucleotides or nucleotide analogs have the structure:

(i)



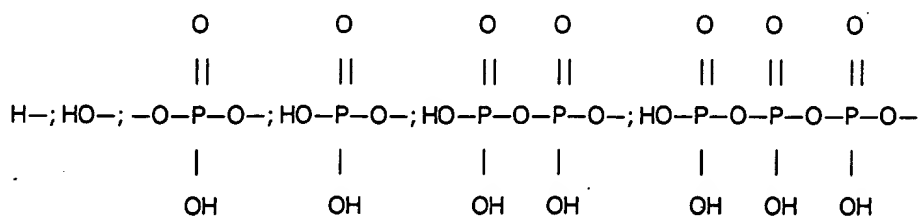
wherein B represents a purine moiety, a 7-deazapurine moiety, a pyrimidine moiety, or an analog of any of the foregoing, and B is covalently bonded to the C1'-position of the sugar moiety or sugar analog, provided that whenever B is a purine, a purine analog, a 7-deazapurine moiety or a 7-deazapurine analog, the sugar moiety or sugar analog is attached at the N9 position of the purine moiety, the purine analog, the 7-deazapurine moiety or the 7-deazapurine analog thereof, and whenever B is a pyrimidine moiety or a pyrimidine analog, the sugar moiety or sugar analog is attached at the N1 position of the pyrimidine moiety or the pyrimidine analog;

wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal; and

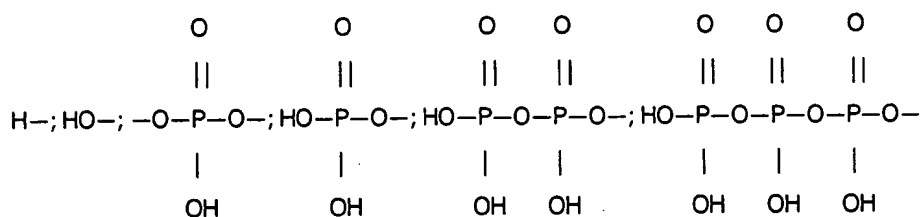
wherein B and A are covalently attached directly or through a linkage group,

wherein if B is a purine or a purine analog, A is attached to the 8-position of the purine or purine analog, if B is a 7-deazapurine or 7-deazapurine analog, A is attached to the 7-position of the deazapurine or deazapurine analog, and if B is a pyrimidine or a pyrimidine analog, A is attached to the 5-position of the pyrimidine or pyrimidine analog; and

wherein x comprises a member selected from the group consisting of:



wherein y comprises a member selected from the group consisting of:



wherein z comprises a member selected from the group consisting of H- and HO-.

1058. (Amended) The process according to claim 1057, wherein y and z [comprise] are [H] H-.

-- 1059. (NEW) The process according to claim 1025, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a mono-phosphate, a di-phosphate, a tri-phosphate and a tetra-phosphate. --

-- 1060. (NEW) The process according to claim 1056, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise a nucleoside mono-, di- or tri-phosphate. --

-- 1061. (NEW) The process according to claims 1025 or 1056, wherein said sugar moiety or sugar analog comprises a monosaccharide. --

-- 1062. (NEW) The process according to claim 1061, wherein said monosaccharide comprises a furanose. --

-- 1063. (NEW) The process according to claim 1062, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose. --

-- 1064. (NEW) The process according to claim 1056, wherein said base moiety or base analog BASE in any of said nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --

-- 1065. (NEW) The process according to claim 1056, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --

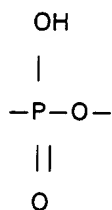
-- 1066. (NEW) The process according to claim 1056, wherein said Sig detectable non-radioactive moiety in said nucleotide M is covalently attached to said BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to BASE at a position when BASE is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof. --

-- 1067. (NEW) The process according to claim 1056, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position selected from the group consisting of the N⁴ position when said pyrimidine comprises cytosine, the N² position when said purine comprises adenine or deazaadenine, the N⁶ position when said purine comprises guanine or deazaguanine, and combinations thereof. --

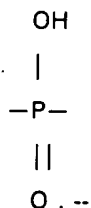
-- 1068. (NEW) The process according to claim 1062, wherein in said nucleotide (ii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 1069. (NEW) The process according to claim 1062, wherein in said nucleotide (iii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 1070. (NEW) The process according to claim 1056, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



and



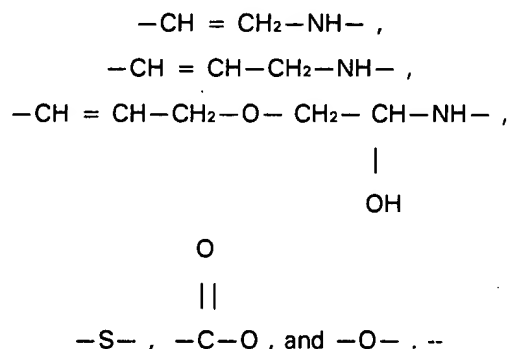
-- 1071. (NEW) The process according to claim 1056, wherein PM is a mono-, di or tri-phosphate, and wherein said nucleotide or nucleotide analog (iii), the Sig moiety is covalently attached to PM through a phosphorus or phosphate oxygen. --

-- 1072. (NEW) The process according to claim 1056, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal. --

-- 1073. (NEW) The process according to claim 1056, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $-\text{CH}_2\text{NH}-$ moiety, or both. --

-- 1074. (NEW) The process according to claim 1056, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group. --

-- 1075. (NEW) The process according to claim 1056, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



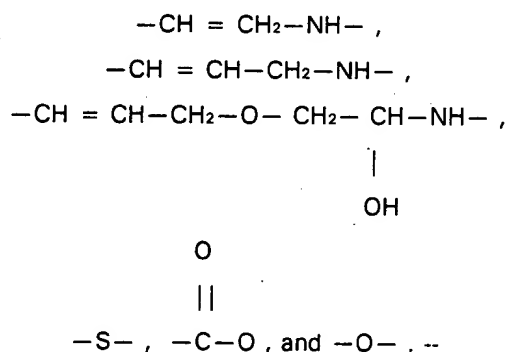
--1076. (NEW) The process according to claim 1056, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety. --

-- 1077. (NEW) The process according to claim 1056, wherein in any of said nucleotides or nucleotide analogs (i), (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group. --

-- 1078. (NEW) The process according to claim 1077, wherein said linkage group contains an amine. --

-- 1079. (NEW) The process according to claim 1078, wherein said amine comprises a primary amine. --

- 1080. (NEW) The process according to claim 1077, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal. --
- 1081. (NEW) The process according to claim 1057, wherein said covalent attachment does not interfere substantially with the characteristic ability of A to form a detectable non-radioactive signal. --
- 1082. (NEW) The process according to claim 1057, wherein said covalent attachment comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $-\text{CH}_2\text{NH}-$ moiety, or both. --
- 1083. (NEW) The process according to claim 1057, wherein said covalent attachment comprises an allylamine group. --
- 1084. (NEW) The process according to claim 1057, wherein said covalent attachment comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



- 1085. (NEW) The process according to claim 1057, wherein said covalent attachment includes a glycosidic linkage moiety. --
- 1086. (NEW) The process according to claim 1057, wherein said A is covalently attached to B through a linkage group. --

-- 1087. (NEW) The process according to claim 1086, wherein said linkage group contains an amine. --

-- 1088. (NEW) The process according to claim 1087, wherein said amine comprises a primary amine. --

-- 1089. (NEW) The process according to claim 1086, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal. --

-- 1090. (NEW) The process according to claim 1056, wherein Sig comprises at least three carbon atoms. --

-- 1091. (NEW) The process according to claim 1056, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --

-- 1092. (NEW) The process according to claim 1056, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms. --

-- 1093. (NEW) The process according to claim 1056, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic moiety comprising at least five carbon atoms. --

-- 1094. (NEW) The process according to claim 1093, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent. --

-- 1095. (NEW) The process according to claim 1056, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --

-- 1096. (NEW) The process according to claim 1095, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent. --

--1097. (NEW) The process according to claim 1056, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide. --

-- 1098. (NEW) The process according to claim 1056, wherein Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --

-- 1099. (NEW) The process according to claim 1098, wherein Sig comprises an electron dense component. --

-- 1100. (NEW) The process according to claim 1099, wherein said electron dense component comprises ferritin. --

-- 1101. (NEW) The process according to claim 1098, wherein Sig comprises a magnetic component. --

-- 1102. (NEW) The process according to claim 1101, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --

-- 1103. (NEW) The process according to claim 1101, wherein said magnetic component comprises magnetic beads. --

-- 1104. (NEW) The process according to claim 1056, wherein Sig comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein. --

-- 1105. (NEW) The process according to claim 1104, wherein the binding protein comprises a lectin. --

-- 1106. (NEW) The process according to claim 1105, wherein the lectin comprises concanavalin A. --

-- 1107. (NEW) The process according to claim 1105, wherein said lectin is conjugated to ferritin. --

- 1108. (NEW) The process according to claim 1098, wherein Sig comprises an enzyme. --
- 1109. (NEW) The process according to claim 1108, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, β -galactosidase, ribonuclease, glucose oxidase, peroxidase, and a combination thereof. --
- 1110. (NEW) The process according to claim 1098, wherein Sig comprises a hormone. --
- 1111. (NEW) The process according to claim 1098, wherein Sig comprises a metal-containing component. --
- 1112. (NEW) The process according to claim 1111, wherein said metal-containing component is catalytic. --
- 1113. (NEW) The process according to claim 1056, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule. --
- 1114. (NEW) The process according to claim 1113, wherein said indicator molecule comprises an aromatic compound. --
- 1115. (NEW) The process according to claim 1114, wherein said aromatic compound is heterocyclic. --
- 1116. (NEW) The process according to claim 1115, wherein said heterocyclic aromatic compound is fluorescent. --
- 1117. (NEW) The process according to claim 1116, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing. --
- 1118. (NEW) The process according to claim 1117, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --

- 1119. (NEW) The process according to claim 1098, wherein Sig comprises a fluorescent component. --
- 1120. (NEW) The process according to claim 1119, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --
- 1121. (NEW) The process according to claim 1120, wherein said fluorescent component comprises fluorescein. --
- 1122. (NEW) The process according to claim 1098, wherein Sig comprises a chemiluminescent component. --
- 1123. (NEW) The process according to claim 1098, wherein Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component. --
- 1124. (NEW) The process according to claim 1098, wherein Sig comprises an antibody component. --
- 1125. (NEW) The process according to claim 1098, wherein Sig comprises a chelating component. --
- 1126. (NEW) The process according to claim 1113, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing. --
- 1127. (NEW) The process according to claim 1057, wherein A comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --
- 1128. (NEW) The process according to claim 1057, wherein A comprises an aliphatic chemical moiety comprising at least four carbon atoms. --

-- 1129. (NEW) The process according to claim 1057, wherein A comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms. --

--1130. (NEW) The process according to claim 1129, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent. --

-- 1131. (NEW) The process according to claim 1057, wherein A comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --

-- 1132. (NEW) The process according to claim 1131, wherein said aromatic or cycloaliphatic group is fluorescent or chemiluminescent. --

-- 1133. (NEW) The process according to claim 1057, wherein A comprises a monosaccharide, polysaccharide or an oligosaccharide. --

-- 1134. (NEW) The process according to claim 1057, wherein A comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --

-- 1135. (NEW) The process according to claim 1134, wherein A comprises an electron dense component. --

-- 1136. (NEW) The process according to claim 1135, wherein said electron dense component comprises ferritin. --

-- 1137. (NEW) The process according to claim 1134, wherein A comprises a magnetic component. --

--1138. (NEW) The process according to claim 1137, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --

-- 1139. (NEW) The process according to claim 1137, wherein said magnetic component comprises magnetic beads. --

- 1140. (NEW) The process according to claim 1057, wherein A comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein. --
- 1141. (NEW) The process according to claim 1140, wherein the binding protein comprises a lectin. --
- 1142. (NEW) The process according to claim 1141, wherein the lectin comprises concanavalin A. --
- 1143. (NEW) The process according to claim 1141, wherein said lectin is conjugated to ferritin. --
- 1144. (NEW) The process according to claim 1134, wherein A comprises an enzyme. --
- 1145. (NEW) The process according to claim 1144, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, β -galactosidase, ribonuclease, glucose oxidase, peroxidase, and a combination thereof. --
- 1146. (NEW) The process according to claim 1134, wherein A comprises a hormone. --
- 1147. (NEW) The process according to claim 1134, wherein A comprises a metal-containing component. --
- 1148. (NEW) The process according to claim 1147, wherein said metal-containing component is catalytic. --
- 1149. (NEW) The process according to claim 1057, wherein said A comprises an indicator molecule. --
- 1150. (NEW) The process according to claim 1149, wherein said indicator molecule comprises an aromatic compound. --

- 1151. (NEW) The process according to claim 1150, wherein said aromatic compound is heterocyclic. --
- 1152. (NEW) The process according to claim 1151, wherein said heterocyclic aromatic compound is fluorescent. --
- 1153. (NEW) The process according to claim 1152, wherein said fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing. --
- 1154. (NEW) The process according to claims 1152 or 1153, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --
- 1155. (NEW) The process according to claim 1154, wherein A comprises a fluorescent component. --
- 1156. (NEW) The process according to claim 1155, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --
- 1157. (NEW) The process according to claim 1156, wherein said fluorescent component comprises fluorescein. --
- 1158. (NEW) The process according to claim 1134, wherein A comprises a chemiluminescent component. --
- 1159. (NEW) The process according to claim 1134, wherein A comprises an antigenic or hapten component capable of completing with an antibody specific to the component. --
- 1160. (NEW) The process according to claim 1134, wherein A comprises an antibody component. --
- 1161. (NEW) The process according to claim 1134, wherein A comprises a chelating component. --

-- 1162. (NEW) The process according to claim 1149, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, a chelating component, and a combination of any of the foregoing. --

1163. (Amended) The process according to claim 1025, wherein said detectable labeled nucleic acid fragments are detectable by a non-radioactive means selected from the group consisting of a fluorescent measurement, a chemiluminescent measurement, and a combination thereof.

1164. (Twice Amended) The process according to claim 1025, wherein said detecting step, the detectable non-radioactive labeled nucleic acid fragments are separated or resolved electrophoretically.

-- 1165. (NEW) The process according to claims 1025, 1056 or 1057, wherein said detecting step is carried out directly. --

-- 1166. (NEW) The process according to claim 1165, wherein said direct detection is carried out using one or more indicator molecules. --

-- 1167. (NEW) The process according to claim 1166, wherein said one or more indicator molecules comprise fluoresceinated nucleotides or nucleotide analogs. --

-- 1168. (NEW) The process according to claim 1167, wherein said fluoresceinated nucleotides or nucleotide analogs comprise fluoresceinated DNA. --

1169. (Amended) The process according to claim 1165, wherein said detecting step is carried out by means of a directly detectable signal provided by said one or more non-radioactive modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

1170. (Amended) The process according to claim 1165, wherein said detecting step the directly detectable signal comprises a member selected from the group consisting of a chelating compound, a fluorogenic compound, [a phosphorescent compound,] a chromogenic compound, a chemiluminescent compound and an electron dense compound.

-- 1171. (NEW) The process according to claim 1165, wherein said detecting step the directly detectable signal comprises an enzyme. --

1172. (Amended) The process according to claims 1025, 1056 or 1057, wherein said detecting step is carried out by means of an indirectly detectable signal provided by said one or more non-radioactive modified or labeled nucleotides or nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

-- 1173. (NEW) The process according to claim 1172, wherein said detecting step the indirectly detectable signal is selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme. --

~~DELETED PER 2ND SUPPL. AMEND. 8/31/00 -- 1174. (NEW) The process according to claim 1172, wherein said detecting step the indirectly detectable signal is provided by a polynucleotide sequence capable of recognizing a signal containing moiety.~~

1175. (Twice Amended) The process according to claim 1025, wherein said one or more modified or labeled nucleotides or nucleotide analogs are capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, [a phosphorescent measurement,] a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

1176. (Twice Amended) The process according to claim 1025, wherein said detecting step comprises localizing said detectable non-radioactive labeled nucleic acid fragments by means of said one or more modified or labeled nucleotides or nucleotide analogs.

1177. (Twice Amended) A process for determining with a sequencing gel the presence of nucleic acid fragments comprising a sequence complementary to a nucleic acid of interest or a portion thereof, said process comprising the steps of:

(A) providing

(i) one or more detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into a nucleic acid; or

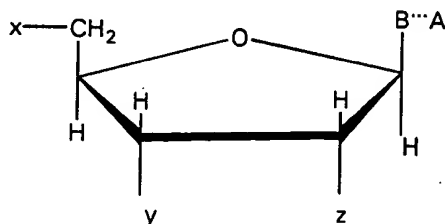
(ii) one or more oligonucleotides or polynucleotides comprising at least one said detectable non-radioactive chemically modified or labeled nucleotide or nucleotide analog; or

(iii) both (i) and (ii);

wherein said detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs (i) and said oligonucleotides and polynucleotides (ii) are capable of attaching to or coupling to or incorporating into or forming one or more nucleic acid fragments, and wherein said detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs have been modified or labeled non-disruptively or disruptively on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety or the base analog thereof; and;

(B) incorporating said one or more detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs (i) or said one or more oligonucleotides or polynucleotides comprising at least one chemically modified or labeled nucleotides or nucleotide analogs (ii), or both (i) and (ii), into one or more nucleic acid fragments, to prepare detectable non-radioactive labeled fragments, each such fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof and said one or more detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs, and wherein said detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

(i)

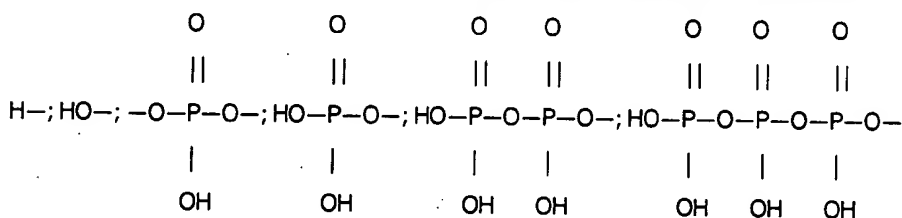


wherein B represents a purine moiety, a 7-deazapurine moiety, a pyrimidine moiety, or an analog of any of the foregoing, and B is covalently bonded to the C1-position of the sugar moiety or sugar analog, provided that whenever B is a purine, a purine analog, a 7-deazapurine moiety or a 7-deazapurine analog, the sugar moiety or sugar analog is attached at the N9 position of the purine moiety, the purine analog, the 7-deazapurine moiety or the 7-deazapurine analog thereof, and whenever B is a pyrimidine moiety or a pyrimidine analog, the sugar moiety or sugar analog is attached at the N1 position of the pyrimidine moiety or the pyrimidine analog;

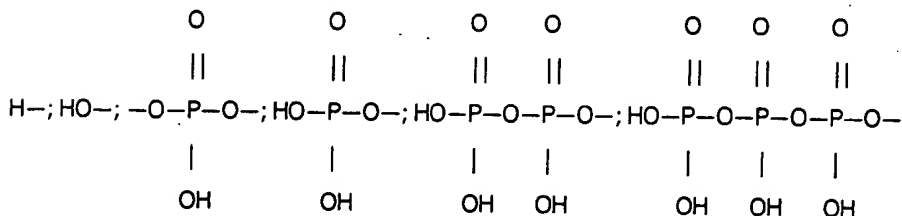
wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal; and

wherein B and A are covalently attached directly or through a linkage group, and

wherein x comprises a member selected from the group consisting of:

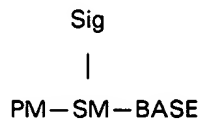


wherein y comprises a member selected from the group consisting of:



wherein z comprises a member selected from the group consisting of H- and
HO-;

(ii)



wherein

PM is a phosphate moiety or phosphate analog,

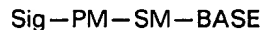
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety, and

wherein said PM is covalently attached to SM, said BASE is covalently attached to
SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii)



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is detectable non-radioactive moiety; and

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
Sig is covalently attached to PM directly or through a linkage group;

(C) transferring or subjecting said detectable non-radioactive labeled
fragments to a sequencing gel;

(D) separating or resolving said detectable non-radioactive labeled
fragments; and

(E) non-radioactively detecting directly or indirectly the presence of said detectable non-radioactive labeled fragments to determine the sequence of said nucleic acid of interest.

-- 1178. (NEW) The process according to claim 1177, wherein the nucleic acid sequence of interest is derived from an organism. --

-- 1179. (NEW) The process according to claim 1178, wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing. --

-- 1180. (NEW) The process according to claim 1179, wherein said organism comprises a mammal. --

-- 1181. (NEW) The process according to claim 1180, wherein said mammal comprises a human being. --

-- 1182. (NEW) The process according to claim 1178, wherein said organism is living. --

-- 1183. (NEW) The process according to claims 1178 or 1182, wherein said organism is selected from the group consisting of prokaryotes and eukaryotes. --

-- 1184. (NEW) The process according to claim 1183, wherein said organism comprises a eukaryote. --

-- 1185. (NEW) The process according to claim 1184, wherein said eukaryotic nucleic acid sequence of interest is contained within a chromosome. --

-- 1186. (NEW) The process according to claim 1184, wherein said eukaryote comprises a mammal. --

-- 1187. (NEW) The process according to claim 1186, wherein said mammalian nucleic acid sequence of interest is contained within a chromosome. --

-- 1188. (NEW) The process according to claim 1186, wherein said mammal comprises a human being. --

-- 1189. (NEW) The process according to claim 1188, wherein said human nucleic acid sequence of interest is contained within a chromosome. --

-- 1190. (NEW) The process according to claim 1189, wherein said human chromosomal nucleic acid sequence of interest is part of a human gene library. --

-- 1191. (NEW) The process according to claim 1177, wherein said incorporating step is carried out using an enzyme. --

-- 1192. (NEW) The process according to claim 1191, wherein said enzyme comprises a polymerase. --

-- 1193. (NEW) The process according to claim 1192, wherein said polymerase comprises DNA polymerase. --

-- 1194. (NEW) The process according to claim 1177, wherein said one or more chemically modified nucleotides or said other modified or unmodified nucleic acids comprise a nucleoside di- or tri-phosphate. --

-- 1195. (NEW) The process according to claim 1177, wherein said incorporating step is template dependent or template independent. --

-- 1196. (NEW) The process according to claim 1177, wherein said incorporating step is template dependent. --

1197. (Amended) The process according to claim 1177, wherein the detectable labeled nucleic acid fragments prepared by said incorporating step comprises at least one internal modified nucleotide.

1198. (Amended) The process according to claim 1177, wherein the detectable labeled nucleic acid fragments prepared by said incorporating step comprises at least one terminal modified nucleotide.

-- 1199. (NEW) The process according to claim 1177, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme. --

-- 1200. (NEW) The process according to claim 1199, wherein said enzyme comprises terminal transferase. --

-- 1201. (NEW) The process according to claim 1177, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling. --

1202. (Wholly Rewritten) The process according to claim 1201, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.

-- 1203. (NEW) The process according to claim 1201, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase. --

-- 1204. (NEW) The process according to claim 1177, wherein said incorporation comprises nick translation. --

-- 1205. (NEW) The process according to claim 1177 or 1204, wherein said incorporation is carried out by means of a polymerizing enzyme. --

-- 1206. (NEW) The process according to claim 1205, wherein said polymerizing enzyme comprises a polymerase. --

-- 1207. (NEW) The process according to claim 1206, wherein said polymerase is selected from the group consisting of DNA polymerase and RNA polymerase. --

-- 1208. (NEW) The process according to claim 1177, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a monophosphate, a di-phosphate, a tri-phosphate and a tetra-phosphate. --

-- 1209. (NEW) The process according to claim 1177, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise a nucleoside mono-, di- or tri-phosphate. --

-- 1210. (NEW) The process according to claim 1177, wherein said sugar moiety or sugar analog comprises a monosaccharide. --

-- 1211. (NEW) The process according to claim 1210, wherein said monosaccharide comprises a furanose. --

-- 1212. (NEW) The process according to claim 1211, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose. --

-- 1213. (NEW) The process according to claim 1177, wherein said B in nucleotide or nucleotide analog (i) or said BASE in nucleotides or nucleotide analogs (ii) or (iii) is selected from the group consisting of a pyrimidine moiety or pyrimidine analog, a purine moiety or purine analog, a 7-deazapurine moiety and a 7-deazapurine analog, and a combination of any of the foregoing. --

-- 1214. (NEW) The process according to claim 1177, wherein in said chemically modified nucleotides or nucleotide analogs (i) when B is a purine or a purine analog, A is attached to the 8-position of the purine moiety or the purine analog, when B is a 7-deazapurine moiety or a 7-deazapurine analog, A is attached to the 7-position of the deazapurine moiety or the 7-deazapurine analog, and when B is a pyrimidine moiety or a pyrimidine analog, A is attached to the 5-position of the pyrimidine moiety or the pyrimidine analog. --

-- 1215. (NEW) The process according to claim 1177, wherein in said chemically modified nucleotides or nucleotide analogs (i) A is covalently attached to said B at a position when B is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to B at a position when B is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof. --

-- 1216. (NEW) The process according to claim 1177, wherein in said chemically modified nucleotides or nucleotide analogs (i) A is covalently attached to said B at a position selected from the group consisting of the N⁴ position when said pyrimidine comprises cytosine, the N² position when said purine comprises adenine or deazaadenine, the N⁶ position when said purine comprises guanine or deazaguanine, and combinations thereof. --

-- 1217. (NEW) The process according to claim 1177, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i) or (iii) or both is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --

-- 1218. (NEW) The process according to claim 1177, wherein said incorporating step, A in the nucleotide (i) is covalently attached to B through a linkage group. --

-- 1219. (NEW) The process according to claim 1218, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal. --

-- 1220. (NEW) The process according to claim 1218, wherein said linkage group contains an amine. --

-- 1221. (NEW) The process according to claim 1220, wherein said amine comprises a primary amine. --

-- 1222. (NEW) The process according to claim 1177, wherein said incorporating step, Sig in the nucleotide (ii) is covalently attached to SM through a linkage group. --

-- 1223. (NEW) The process according to claim 1222, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal. --

-- 1224. (NEW) The process according to claim 1222, wherein said linkage group contains an amine. --

-- 1225. (NEW) The process according to claim 1224, wherein said amine comprises a primary amine. --

-- 1226. (NEW) The process according to claim 1177, wherein said incorporating step, Sig in the nucleotide (iii) is covalently attached to PM through a linkage group. --

-- 1227. (NEW) The process according to claim 1226, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal. --

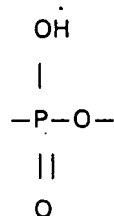
-- 1228. (NEW) The process according to claim 1226, wherein said linkage group contains an amine. --

-- 1229. (NEW) The process according to claim 1228, wherein said amine comprises a primary amine. --

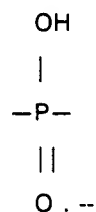
-- 1230. (NEW) The process according to claim 1211, wherein in said nucleotide (ii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 1231. (NEW) The process according to claim 1211, wherein in said nucleotide (iii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 1232. (NEW) The process according to claim 1177, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



and



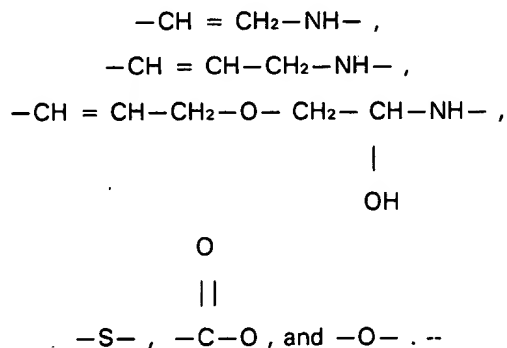
-- 1233. (NEW) The process according to claim 1177, wherein PM is a mono-, di- or tri-phosphate, and wherein in said nucleotide or nucleotide analog (iii), the Sig moiety is covalently attached to PM through a phosphorus or phosphate oxygen. --

-- 1234. (NEW) The process according to claim 1177, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of A or Sig to form a detectable non-radioactive signal. --

1235. (Amended) The process according to claim 1177, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $[-\text{CH}_2\text{NH}-]$ $-\text{CH}_2\text{NH}-$ moiety, or both.

-- 1236. (NEW) The process according to claim 1177, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group. --

-- 1237. (NEW) The process according to claim 1177, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



-- 1238. (NEW) The process according to claim 1177, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety. --

-- 1239. (NEW) The process according to claim 1177, wherein in said nucleotides or nucleotide analogs (i), A is covalently attached to B through a linkage group, or in said nucleotides or nucleotide analogs (ii) or (iii), Sig is covalently attached to BASE, SM or PM through a linkage group. --

-- 1240. (NEW) The process according to claim 1239, wherein said linkage group contains an amine. --

-- 1241. (NEW) The process according to claim 1240, wherein said amine comprises a primary amine. --

-- 1242. (NEW) The process according to claim 1239, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal. --

-- 1243. (NEW) The process according to claim 1177, wherein said A or Sig comprises at least three carbon atoms. --

-- 1244. (NEW) The process according to claim 1177, wherein said A or Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --

-- 1245. (NEW) The process according to claim 1177, wherein said A or Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms. --

-- 1246. (NEW) The process according to claim 1177, wherein said A or Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms. --

-- 1247. (NEW) The process according to claim 1141, wherein said A or Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --

-- 1248. (NEW) The process according to claim 1177, wherein said A or Sig comprises a monosaccharide, polysaccharide or an oligosaccharide. --

-- 1249. (NEW) The process according to claim 1177, wherein said A or Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --

-- 1250. (NEW) The process according to claim 1249, wherein said A or Sig comprises an electron dense component. --

-- 1251. (NEW) The process according to claim 1250, wherein said electron dense component comprises ferritin. --

-- 1252. (NEW) The process according to claim 1249, wherein said A or Sig comprises a magnetic component. --

- 1253. (NEW) The process according to claim 1252, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --
- 1254. (NEW) The process according to claim 1252, wherein said magnetic component comprises magnetic beads. --
- 1255. (NEW) The process according to claim 1177, wherein said A or Sig comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein. --
- 1256.. (NEW) The process according to claim 1255, wherein the binding protein comprises a lectin. --
- 1257. (NEW) The process according to claim 1256, wherein the lectin comprises concanavalin A. --
- 1258. (NEW) The process according to claim 1256, wherein said lectin is conjugated to ferritin. --
- 1259. (NEW) The process according to claim 1249, wherein said A or Sig comprises an enzyme. --
- 1260. (NEW) The process according to claim 1259, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, β -galactosidase, ribonuclease, glucose oxidase and peroxidase, or a combination thereof. --
- 1261. (NEW) The process according to claim 1249, wherein said A or Sig comprises a hormone. --
- 1262. (NEW) The process according to claim 1249, wherein said A or Sig comprises a metal-containing component. --
- 1263. (NEW) The process according to claim 1262, wherein said metal-containing component is catalytic. --

- 1264. (NEW) The process according to claim 1177, wherein said A or Sig detectable non-radioactive moiety comprises an indicator molecule. --
- 1265. (NEW) The process according to claim 1264, wherein said indicator molecule comprises an aromatic compound. --
- 1266. (NEW) The process according to claim 1265, wherein said aromatic compound is heterocyclic. --
- 1267. (NEW) The process according to claim 1266, wherein said heterocyclic aromatic compound is fluorescent. --
- 1268. (NEW) The process according to claim 1267, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine and dansyl. --
- 1269. (NEW) The process according to claim 1268, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --
- 1270. (NEW) The process according to claim 1264, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, and a chelating component, or a combination of any of the foregoing. --
- 1271. (NEW) The process according to claim 1249, wherein said A or Sig comprises a fluorescent component. --
- 1272. (NEW) The process according to claim 1271, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --
- 1273. (NEW) The process according to claim 1272, wherein said fluorescent component comprises fluorescein. --
- 1274. (NEW) The process according to claim 1249, wherein said A or Sig comprises a chemiluminescent component. --

- 1275. (NEW) The process according to claim 1249, wherein said A or Sig comprises an antigenic or hapten component capable of completing with an antibody specific to the component. --
- 1276. (NEW) The process according to claim 1249, wherein said A or Sig comprises an antibody component. --
- 1277. (NEW) The process according to claim 1249, wherein said A or Sig comprises a chelating component. --
- 1278. (NEW) The process according to claim 1177, wherein any of nucleotide or nucleotide analogs (i), (ii) and (iii) are detectable by a means selected from the group consisting of a fluorescent measurement and a chemiluminescent measurement, or a combination thereof. --
- 1279. (NEW) The process according to claim 1177, wherein said A or Sig is detectable when it is attached to the nucleotide or nucleotide analog directly or through a linkage group. --
- 1280. (NEW) The process according to claim 1279, wherein said linkage group does not interfere substantially with the characteristic ability of A or Sig to form a detectable non-radioactive signal. --
1281. (Twice Amended) The process according to claim 1177, wherein said detectable non-radioactive labeled nucleic acid fragment or fragments are terminally ligated or attached to a polypeptide.
- 1282. (NEW) The process according to claim 1281, wherein the polypeptide comprises a polylysine. --
- 1283. (NEW) The process according to claim 1281, wherein the polypeptide comprises at least one member selected from the group consisting of avidin, streptavidin or anti-Sig immunoglobulin. --

-- 1284. (NEW) The process according to claim 1281, wherein said A or Sig comprises a ligand and the polypeptide comprises an antibody thereto. --

-- 1285. (NEW) The process according to claim 1177, wherein said separating step is carried out electrophoretically. --

-- 1286. (NEW) The process according to claim 1177, wherein said detecting step is carried out directly. --

-- 1287. (NEW) The process according to claim 1286, wherein said direct detection is carried out on one or more indicator molecules. --

-- 1288. (NEW) The process according to claim 1287, wherein said one or more indicator molecules comprise fluoresceinated nucleotides. --

-- 1289. (NEW) The process according to claim 1288, wherein said fluoresceinated nucleotides or nucleotide analogs comprise fluoresceinated DNA. --

-- 1290. (NEW) The process according to claim 1177, wherein said detecting step is carried out by means of a directly detectable signal provided by said A or Sig detectable non-radioactive moiety. --

1291. (Amended) The process according to claim 1290, wherein said detecting step the directly detectable signal providing A or Sig detectable non-radioactive moiety comprises a member selected from the group consisting of a fluorogenic compound, [a phosphorescent compound,] a chromogenic compound, a chemiluminescent compound and an electron dense compound.

-- 1292. (NEW) The process according to claim 1290, wherein said detecting step the directly detectable signal is provided by an enzyme. --

-- 1293. (NEW) The process according to claim 1177, wherein said detecting step is carried out by means of an indirectly detectable signal provided by said A or Sig detectable non-radioactive moiety. --

-- 1294. (NEW) The process according to claim 1293, wherein said detecting step the indirectly detectable signal is provided by a member selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme. --

~~DELETED PER 2ND SUPPL. AMEND. 8/31/00 -- 1295. (NEW) The process according to claim 1293, wherein said detecting step the indirectly detectable signal providing Sig detectable non-radioactive moiety comprises a polynucleotide sequence capable of recognizing a signal containing moiety. --~~

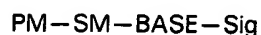
-- 1296. (NEW) The process according to claim 1293, wherein said detecting step the indirectly detectable signal providing Sig detectable non-radioactive moiety comprises a compound capable of binding to an insoluble phase. --

1297. (Twice Amended) The process according to claim 1177, wherein said Sig detectable non-radioactive moiety is capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, [a phosphorescent measurement,] a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

1298. (Twice Amended) A process for detecting a nucleic acid of interest in a sample, which process comprises the steps of:

(a) specifically hybridizing said nucleic acid of interest in the sample with one or more detectable non-radioactive labeled oligo- or polynucleotides, each such oligo- or polynucleotide being complementary to or capable of hybridizing with said nucleic acid of interest or a portion thereof, wherein said oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said detectable non-radioactive modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

(i) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

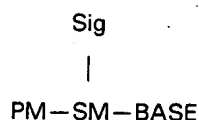
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety or a base analog of any of the foregoing; and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof, and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization;

(ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

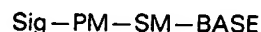
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization; and

(iii) a nucleotide or nucleotide analog, said nucleotide having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group, and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization;

provided that when said nucleotide or nucleotide analog (iii) is attached to an oligoribonucleotide or a polyribonucleotide, and provided that when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide; and

(b) detecting non-radioactively the presence of said Sig detectable non-radioactive moieties in any of the detectable non-radioactive labeled oligo- or polynucleotides which have hybridized to said nucleic acid of interest.

-- 1299. (NEW) The process according to claim 1298, wherein the nucleic acid of interest comprises DNA, RNA or a DNA-RNA hybrid. --

-- 1300. (NEW) The process according to claim 1298, wherein the nucleic acid of interest is double-stranded or single-stranded. --

-- 1301. (NEW) The process according to claim 1298, wherein the nucleic acid of interest has been rendered single-stranded. --

-- 1302. (NEW) The process according to claim 1298, wherein the nucleic acid of interest is derived from an organism. --

-- 1303. (NEW) The process according to claim 1302, wherein the organism is selected from the group consisting of prokaryotes and eukaryotes. --

-- 1304. (NEW) The process according to claim 1302, wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing. --

- 1305. (NEW) The process according to claim 1302, wherein said organism is living. --
- 1306. (NEW) The process according to claim 1298, wherein the sample is suspected of containing an etiological agent and the nucleic acid of interest is naturally associated with the etiological agent. --
- 1307. (NEW) The process according to claim 1306, wherein the sample is of human or animal origin and the etiological agent is selected from the group consisting of bacteria, virus and fungi. --
- 1308. (NEW) The process according to claim 1298, wherein said nucleic acid of interest is derived from a member selected from the group consisting of *Streptococcus pyrogenes*, *Neisseria meningitidis*, *Staphylococcus aureus*, *Candida albicans*, *Pseudomonas aeruginosa*, *Neisseria gonorrhoeae*, *Mycobacterium tuberculosis*, and any combinations of the foregoing. --
- 1309. (NEW) The process according to claim 1298, wherein said one or more oligo- or polynucleotides are derived from *Neisseria gonorrhoeae*. --
- 1310. (NEW) The process according to claim 1298, wherein the sample comprises a bacterium suspected of containing a nucleic acid of interest which imparts resistance to an antibiotic and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the sequence of the bacterium which confers resistance to the antibiotic. --
- 1311. (NEW) The process according to claim 1310, wherein when said bacterium is *Streptococcus pyrogenes* or *Neisseria meningitidis*, said antibiotic is penicillin, wherein when said bacterium is *Staphylococcus aureus*, *Candida albicans*, *Pseudomonas aeruginosa*, *Streptococcus pyrogenes*, or *Neisseria gonorrhoeae*, said antibiotic is a tetracycline, and wherein when said bacterium is *Mycobacterium tuberculosis*, said antibiotic is an aminoglycoside. --
- 1312. (NEW) The process according to claim 1311, wherein said bacterium is *Neisseria gonorrhoeae* and said antibiotic is selected from the group consisting of penicillin, tetracycline, aminoglycoside and combinations thereof. --

-- 1313. (NEW) The process according to claim 1298, wherein the sample is suspected of containing a nucleic acid of interest associated with a genetic disorder and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the nucleic acid associated with the genetic disorder. --

-- 1314. (NEW) The process according to claim 1298, wherein the sample is suspected of containing a nucleic acid of interest associated with thalassemia and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the nucleic acid which is absent in the thalassemic subjects. --

-- 1315. (NEW) The process according to claim 1298, wherein said process is utilized for chromosomal karyotyping which comprises contacting the sample with a series of the oligo- or polynucleotides which are complementary to a series of known genetic sequences located on chromosomes. --

-- 1316. (NEW) The process according to claim 1298, wherein the sample is suspected of containing a nucleic acid which includes a terminal polynucleotide sequence poly A and wherein the oligo- or polynucleotide comprises a modified poly U molecule in which at least one uracil moiety has been modified by chemical addition of Sig to the 5' position of said uracil moiety. --

-- 1317. (NEW) The process according to claim 1298, wherein said process is utilized to determine the number of copies of an individual chromosome in a sample. --

-- 1318. (NEW) The process according to claim 1298, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme. --

-- 1319. (NEW) The process according to claim 1318, wherein said enzyme comprises terminal transferase. --

-- 1320. (NEW) The process according to claim 1298, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling. --

1321. (Wholly Rewritten) The process according to claim 1320, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.

--1322. (NEW) The process according to claim 1320, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase. --

-- 1323. (NEW) The process according to claim 1298, wherein said incorporation comprises nick translation. --

-- 1324. (NEW) The process according to claim 1298 or 1323, wherein said incorporation is carried out by means of a polymerizing enzyme. --

-- 1325. (NEW) The process according to claim 1324, wherein said polymerizing enzyme comprises a polymerase. --

-- 1326. (NEW) The process according to claim 1325, wherein said polymerase is selected from the group consisting of DNA polymerase and RNA polymerase. --

-- 1327. (NEW) The process according to claim 1298, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a monophosphate, a di-phosphate, a tri-phosphate and a tetra-phosphate. --

-- 1328. (NEW) The process according to claim 1298, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise a nucleoside mono-, di- or tri-phosphate. --

-- 1329. (NEW) The process according to claim 1298, wherein said sugar moiety or sugar analog comprises a monosaccharide. --

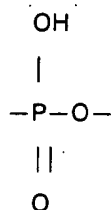
-- 1330. (NEW) The process according to claim 1329, wherein said monosaccharide comprises a furanose. --

-- 1331. (NEW) The process according to claim 1330, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose. --

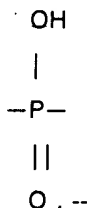
- 1332. (NEW) The process according to claim 1298, wherein said base moiety or base analog BASE in any of said nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --
- 1333. (NEW) The process according to claim 1298, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --
- 1334. (NEW) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to BASE at a position when BASE is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof. --
- 1335. (NEW) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position selected from the group consisting of the N⁴ position when said pyrimidine comprises cytosine, the N² position when said purine comprises adenine or deazaadenine, the N⁶ position when said purine comprises guanine or deazaguanine, and combinations thereof. --
- 1336. (NEW) The process according to claim 1333, wherein in said nucleotide (ii), PM is attached to said monosaccharide or furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 1337. (NEW) The process according to claim 1333, wherein in said nucleotide (iii), PM is attached to said monosaccharide or furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said monosaccharide or furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 1338. (NEW) The process according to claim 1298, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



and



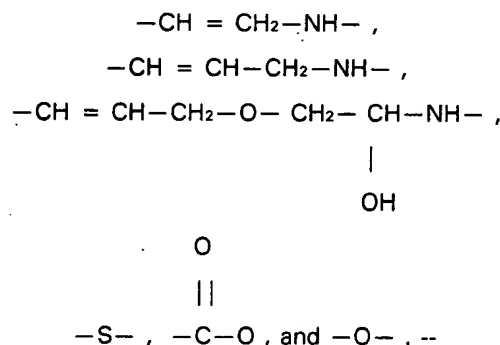
-- 1339. (NEW) The process according to claim 1298, wherein PM is a mono-, di or tri-phosphate, and wherein said nucleotide or nucleotide analog (iii), the Sig detectable non-radioactive moiety is covalently attached to PM through a phosphorus or phosphate oxygen. --

1340. (Amended) The process according to claim 1298, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal.

-- 1341. (NEW) The process according to claim 1298, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $-\text{CH}_2\text{NH}-$ moiety, or both. --

-- 1342. (NEW) The process according to claim 1298, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group. --

-- 1343. (NEW) The process according to claim 1298, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



-- 1344. (NEW) The process according to claim 1298, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety. --

-- 1345. (NEW) The process according to claim 1298, wherein in any of said nucleotides or nucleotide analogs (i), (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group. --

-- 1346. (NEW) The process according to claim 1345, wherein said linkage group contains an amine. --

-- 1347. (NEW) The process according to claim 1346, wherein said amine comprises a primary amine. --

-- 1348. (NEW) The process according to claim 1345, wherein said linkage group does not substantially interfere with nucleic acid hybridization or double-stranded nucleic acid formation. --

1349. (Amended) The process according to claim 1345, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

-- 1350. (NEW) The process according to claim 1298, wherein Sig comprises at least three carbon atoms. --

-- 1351. (NEW) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --

-- 1352. (NEW) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms. --

-- 1353. (NEW) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms. --

-- 1354. (NEW) The process according to claim 1353, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent. --

-- 1355. (NEW) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --

-- 1356. (NEW) The process according to claim 1355, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent. --

-- 1357. (NEW) The process according to claim 1298, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide. --

-- 1358. (NEW) The process according to claim 1298, wherein Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --

-- 1359. (NEW) The process according to claim 1358, wherein Sig comprises an electron dense component. --

-- 1360. (NEW) The process according to claim 1359, wherein said electron dense component comprises ferritin. --

-- 1361. (NEW) The process according to claim 1358, wherein Sig comprises a magnetic component. --

-- 1362. (NEW) The process according to claim 1361, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --

-- 1363. (NEW) The process according to claim 1361, wherein said magnetic component comprises magnetic beads. --

-- 1364. (NEW) The process according to claim 1298, wherein Sig comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein. --

-- 1365. (NEW) The process according to claim 1364, wherein the binding protein comprises a lectin. --

-- 1366. (NEW) The process according to claim 1365, wherein the lectin comprises concanavalin A. --

-- 1367. (NEW) The process according to claim 1365, wherein said lectin is conjugated to ferritin. --

-- 1368. (NEW) The process according to claim 1358, wherein Sig comprises an enzyme. --

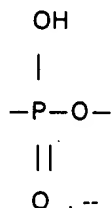
- 1369. (NEW) The process according to claim 1368, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, β -galactosidase, ribonuclease, glucose oxidase and peroxidase, or a combination thereof. --
- 1370. (NEW) The process according to claim 1358, wherein Sig comprises a hormone. --
- 1371. (NEW) The process according to claim 1358, wherein Sig comprises a metal-containing component. --
- 1372. (NEW) The process according to claim 1371, wherein said metal-containing component is catalytic. --
- 1373. (NEW) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule. --
- 1374. (NEW) The process according to claim 1373, wherein said indicator molecule comprises an aromatic compound. --
- 1375. (NEW) The process according to claim 1374, wherein said aromatic compound is heterocyclic. --
- 1376. (NEW) The process according to claim 1375, wherein said heterocyclic aromatic compound is fluorescent. --
- 1377. (NEW) The process according to claim 1376, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing. --
- 1378. (NEW) The process according to claim 1377, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --
- 1379. (NEW) The process according to claim 1358, wherein Sig comprises a fluorescent component. --

- 1380. (NEW) The process according to claim 1379, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --
- 1381. (NEW) The process according to claim 1380, wherein said fluorescent component comprises fluorescein. --
- 1382. (NEW) The process according to claim 1358 wherein Sig comprises a chemiluminescent component. --
- 1383. (NEW) The process according to claim 1358, wherein Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component. --
- 1384. (NEW) The process according to claim 1358, wherein Sig comprises an antibody component. --
- 1385. (NEW) The process according to claim 1358, wherein Sig comprises a chelating component. --
- 1386. (NEW) The process according to claim 1373, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, and a chelating component, or a combination of any of the foregoing. --
- 1387. (NEW) The process according to claim 1298, wherein any of nucleotide or nucleotide analogs (i), (ii) and (iii) are detectable by a means selected from the group consisting of a fluorescent measurement and a chemiluminescent measurement, or a combination thereof. --
- 1388. (NEW) The process according to claim 1298, wherein Sig is detectable non-radioactively when the oligo- or polynucleotide is contained in a double-stranded ribonucleic or deoxyribonucleic acid duplex. --

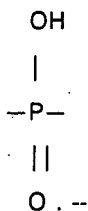
-- 1389. (NEW) The process according to claim 1298, wherein Sig is detectable non-radioactively when it is attached to the nucleotide directly or through a linkage group. --

-- 1390. (NEW) The process according to claim 1389, wherein said linkage group does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal. --

-- 1391. (NEW) The process according to claim 1298, wherein Sig in said nucleotide (iii) is covalently attached to PM via the chemical linkage



-- 1392. (NEW) The process according to claim 1298, wherein Sig in said nucleotide (iii) is covalently attached to PM via the chemical linkage



1393. (Amended) The process according to claim 1298, wherein the [oligo-or] oligo- or polynucleotide is terminally ligated or attached to a polypeptide.

-- 1394. (NEW) The process according to claim 1298, further comprising contacting the sample with a polypeptide capable of forming a complex with Sig and a moiety which can be detected when the complex is formed. --

-- 1395. (NEW) The process according to claims 1393 or 1394, wherein the polypeptide comprises a polylysine. --

- 1396. (NEW) The process according to claims 1393 or 1394, wherein the polypeptide comprises at least one member selected from the group consisting of avidin, streptavidin or anti-Sig immunoglobulin. --
- 1397. (NEW) The process according to claim 1394, wherein Sig comprises a ligand and the polypeptide comprises an antibody thereto. --
- 1398. (NEW) The process according to claim 1394, wherein the moiety which can be detected when the complex is formed is selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --
- 1399. (NEW) The process according to claim 1298, wherein said detecting step is carried out directly. --
- 1400. (NEW) The process according to claim 1399, wherein said direct detection is carried out on one or more nucleotides or nucleotide analogs comprising indicator molecules. --
- 1401. (NEW) The process according to claim 1400, wherein said one or more indicator molecules comprise fluoresceinated nucleotides. --
- 1402. (NEW) The process according to claim 1401, wherein said fluoresceinated nucleotides or nucleotide analogs comprise fluoresceinated DNA. --
- 1403. (NEW) The process according to claim 1298, wherein said detecting step is carried out by means of a directly detectable non-radioactive signal provided by said Sig detectable non-radioactive moiety. --
- 1404. (NEW) The process according to claim 1403, wherein said detecting step the directly detectable non-radioactive signal comprises a member selected from the group consisting of a fluorogenic compound, a phosphorescent compound, a chromogenic compound, a chemiluminescent compound and an electron dense compound. --

1405. (Amended) The process according to claim 1403, wherein said detecting step the directly detectable non-radioactive signal is provided by an enzyme.

-- 1406. (NEW) The process according to claim 1298, wherein said detecting step is carried out by means of a indirectly detectable non-radioactive signal provided by said Sig detectable non-radioactive moiety. --

-- 1407. (NEW) The process according to claim 1406, wherein said detecting step the indirectly detectable non-radioactive signal is selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme. --

~~DELETED PER 2ND SUPPL. AMEND. 8/31/00 -- 1408. (NEW) The process according to claim 1406, wherein said detecting step the indirectly detectable non-radioactive signal comprises a polynucleotide sequence capable of recognizing a signal containing moiety. --~~

1409. (Twice Amended) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety is capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, [a phosphorescent measurement,] a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

-- 1410. (NEW) The process according to claim 1255, further comprising one or more washing steps. --

1411. (Twice Amended) A process for detecting a nucleic acid of interest in a sample, which process comprises the steps of:

(A) providing:

(i) an oligo- or polynucleotide [having two segments:

(a) a first segment] complementary to and capable of
(1) specifically hybridizing to and forming a hybrid with a
nucleic acid of interest or a portion thereof and (2)
capable of binding to or complexing with a non-
radioactively detectable protein [of said nucleic acid of
interest; and

(b) a second segment comprising at least one protein
binding nucleic acid sequence]; and

(ii) a non-radioactively detectable protein which is capable of
binding to or complexing with said nucleic acid hybrid [protein binding
nucleic acid sequence];

(B) contacting a sample suspected of containing said nucleic acid of
interest with said oligo- or polynucleotide (i) and said non-radioactively detectable
protein (ii) to form a complex; and

(C) detecting non-radioactively the presence of said non-radioactively
detectable protein in said complex [and] to detect said nucleic acid of interest.

-- 1412. (NEW) The process according to claim 1411, wherein the nucleic acid of
interest comprises DNA, RNA or a DNA-RNA hybrid. --

-- 1413. (NEW) The process according to claim 1411, wherein the nucleic acid of
interest is double-stranded or single-stranded. --

-- 1414. (NEW) The process according to claim 1411, wherein the nucleic acid of
interest has been rendered single-stranded. --

-- 1415. (NEW) The process according to claim 1411, wherein the nucleic acid of
interest is derived from an organism. --

-- 1416. (NEW) The process according to claim 1415, wherein the living organism
is selected from the group consisting of prokaryotes and eukaryotes. --

-- 1417. (NEW) The process according to claim 1415, wherein said organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing. --

-- 1418. (NEW) The process according to claim 1415, wherein said organism is living. --

-- 1419. (NEW) The process according to claim 1411, wherein the sample is suspected of containing an etiological agent and the nucleic acid of interest is naturally associated with the etiological agent. --

-- 1420. (NEW) The process according to claim 1419, wherein the sample is of human or animal origin and the etiological agent is selected from the group consisting of bacteria, virus and fungi. --

-- 1421. (NEW) The process according to claim 1411, wherein said nucleic acid of interest are derived from a member selected from the group consisting of *Streptococcus pyrogenes*, *Neisseria meningitides*, *Staphylococcus aureus*, *Candida albicans*, *Pseudomonas aeruginosa*, *Neisseria gonorrhoeae*, *Mycobacterium tuberculosis*, and any combinations of the foregoing. --

-- 1422. (NEW) The process according to claim 1411, wherein said one or more oligo- or polynucleotides are derived from *Neisseria gonorrhoeae*. --

-- 1423. (NEW) The process according to claim 1411, wherein the sample comprises a bacterium suspected of containing a nucleic acid of interest which imparts resistance to an antibiotic and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the sequence of the bacterium which confers resistance to the antibiotic. --

-- 1424. (NEW) The process according to claim 1423, wherein when said bacterium is *Streptococcus pyrogenes* or *Neisseria meningitidis*, said antibiotic is penicillin, wherein when said bacterium is *Staphylococcus aureus*, *Candida albicans*, *Pseudomonas aeruginosa*, *Streptococcus pyrogenes*, or *Neisseria gonorrhoea*, said antibiotic is a tetracycline, and wherein when said bacterium is *Mycobacterium tuberculosis*, said antibiotic is an aminoglycoside. --

-- 1425. (NEW) The process according to claim 1424, wherein said bacterium is *Neisseria gonorrhoeae* and said antibiotic is selected from the group consisting of penicillin, tetracycline, aminoglycoside and combinations thereof. --

-- 1426. (NEW) The process according to claim 1411, wherein the sample is suspected of containing a nucleic acid of interest associated with a genetic disorder and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the nucleic acid associated with the genetic disorder. --

--1427. (NEW) The process according to claim 1411, wherein the sample is suspected of containing a nucleic acid of interest associated with thalassemia and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the nucleic acid which is absent in the thalassemic subjects. --

-- 1428. (NEW) The process according to claim 1411, wherein said process is utilized for chromosomal karyotyping which comprises contacting the sample with a series of the oligo- or polynucleotides (i) which are complementary to a series of known genetic sequences located on chromosomes. --

-- 1429. (NEW) The process according to claim 1411, wherein said process is utilized to determine the number of copies of an individual chromosome in a sample. --

1430. (Amended) The process according to claim 1411, wherein said oligo- or polynucleotide (i) comprises at least one protein binding nucleic acid sequence [is] selected from the group consisting of an antibody, a promoter, a repressor and an inducer.

-- 1431. (NEW) The process according to claim 1430, wherein said repressor comprises a lac repressor. --

1432. (Amended) The process according to claim [1411] 1430, wherein said at least one protein binding nucleic acid sequence is covalently attached to said oligo- or polynucleotide.

-- 1433. (NEW) The process according to claim 1432, wherein said covalent attachment comprises ligation. --

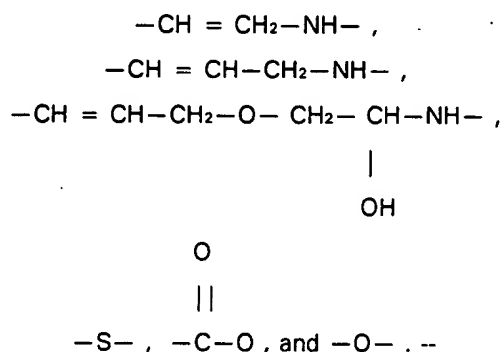
1434. (Amended) The process according to claim 1432, wherein said covalent attachment does not interfere substantially with the characteristic ability of said non-radioactively detectable protein to bind to any hybrid formed between said oligo- or polynucleotide (i) and said nucleic acid of interest.

1435. (Amended) The process according to claim 1432, wherein said covalent attachment does not interfere substantially with the characteristic ability of said non-radioactively detectable protein to be detected non-radioactively when bound to any hybrid formed between said oligo- or polynucleotide (i) and said nucleic acid of interest.

-- 1436. (NEW) The process according to claim 1432, wherein said covalent attachment comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $\text{CH}_2\text{NH}-$ moiety, or both. --

1437. (NEW) The process according to claim 1436, wherein said covalent attachment comprises an allylamine group. --

--1438. (NEW) The process according to claim 1436, wherein said covalent attachment comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



--1439. (NEW) The process according to claim 1432, wherein said covalent attachment includes a glycosidic linkage moiety. --

-- 1440. (NEW) The process according to claim 1432, wherein said protein binding sequence is covalently attached to any of the base, phosphate, or sugar moieties in said oligo- or polynucleotide. --

-- 1441. (NEW) The process according to claim 1440, wherein said covalent attachment is through a linkage group. --

-- 1442. (NEW) The process according to claim 1441, wherein said linkage group contains an amine. --

-- 1443. (NEW) The process according to claim 1442, wherein said amine comprises a primary amine. --

-- 1444. (NEW) The process according to claim 1441, wherein said linkage group does not substantially interfere with the binding of said non-radioactively detectable protein to said protein binding sequence. --

-- 1445. (NEW) The process according to claim 1411, wherein said non-radioactively detectable protein comprises a signaling component or indicator molecule. --

-- 1446. (NEW) The process according to claim 1445, wherein said signaling component or indicator molecule comprises at least three carbon atoms. --

-- 1447. (NEW) The process according to claim 1446, wherein said signaling component or indicator molecule comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --

1448. (Amended) The process according to claim 1446, [Wherein] wherein said signaling component or indicator molecule comprises an aliphatic chemical moiety comprising at least four carbon atoms.

-- 1449. (NEW) The process according to claim 1446, wherein said signaling component or indicator molecule comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms. --

-- 1450. (NEW) The process according to claim 1449, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent. --

-- 1451. (NEW) The process according to claim 1446, wherein said signaling component or indicator molecule comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --

-- 1452. (NEW) The process according to claim 1451, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent. --

1453. (Amended) The process according to claim 1446, wherein said signaling component or indicator molecule comprises a monosaccharide, polysaccharide or an oligosaccharide.

-- 1454. (NEW) The process according to claim 1445, wherein said signaling component or indicator molecule comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --

- 1455. (NEW) The process according to claim 1445, wherein said signaling component or indicator molecule comprises an aromatic compound. --
- 1456. (NEW) The process according to claim 1455, wherein said aromatic compound is heterocyclic. --
- 1457. (NEW) The process according to claim 1456, wherein said heterocyclic aromatic compound is fluorescent. --
- 1458. (NEW) The process according to claim 1457, wherein said fluorescent heterocyclic aromatic compounds is selected from the group consisting of fluorescein, rhodamine and dansyl. --
- 1459. (NEW) The process according to claim 1458, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --
- 1460. (NEW) The process according to claim 1454, wherein said signaling component or indicator molecule comprises a chemiluminescent component. --
- 1461. (NEW) The process according to claim 1454, wherein said signaling component or indicator molecule comprises a chelating component. --
- 1462. (NEW) The process according to claim 1411, wherein said non-radioactively detectable protein is detectable by a means selected from the group consisting of a fluorescent measurement and a chemiluminescent measurement, or a combination thereof. --
- 1463. (NEW) The process according to claim 1411, wherein said non-radioactively detectable protein is detectable when the oligo- or polynucleotide (i) is contained in a double-stranded ribonucleic or deoxyribonucleic acid duplex formed with said nucleic acid of interest. --
- 1464. (NEW) The process according to claim 1411, wherein said nonradioactively detectable protein is detectable when it is attached to said oligo- or polynucleotide (i) directly or through a linkage group. --

-- 1465. (NEW) The process according to claim 1411, wherein said oligo- or polynucleotide (i) is contacted with said sample suspected of containing the nucleic acid of interest prior to forming a complex with said non-radioactively detectable protein. --

-- 1466. (NEW) The process according to claim 1411, wherein said detecting step is carried out directly. --

-- 1467. (NEW) The process according to claim 1466, wherein said direct detection of the non-radioactively detectable protein is carried out on one or more signaling components or indicator molecules. --

1468. (Amended) The process according to claims 1467, wherein said direct detection step is carried out by a member selected from the group consisting of a fluorogenic compound, [a phosphorescent compound,] a chromogenic compound, a chemiluminescent compound, an enzyme, a radioactive compound and an electron dense compound.

-- 1469. (NEW) The process according to claim 1411, wherein said detecting step is carried out indirectly. --

1470. (Wholly Rewritten) The process according to claim 1469, wherein said indirect detection is carried out by a means selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme, a compound capable of binding to an insoluble phase, and a combination of any of the foregoing.

1471. (Twice Amended) The process according to claim 1411, wherein said nonradioactively detectable protein is capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, [a phosphorescent measurement,] a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

-- 1472. (NEW) The process according to claim 1411, further comprising one or more washing steps. --

1473. (Amended) A process for determining whether the number of copies of a particular chromosome in a cell is normal or abnormal, the process comprising the steps of:

contacting said cell under hybridizing conditions with one or more clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are capable of hybridizing specifically to a locus or loci of said particular chromosome or a portion thereof, wherein said clones or fragments or oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said detectable non-radioactive modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

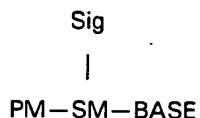
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety or an analog of any of the foregoing thereof, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to the SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof, and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

(ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

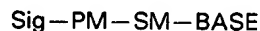
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to
SM, and Sig is covalently attached to PM directly or through a linkage group,

to permit specific hybridization of said clone or clones or DNA fragments or oligo-
or polynucleotides to the locus or loci of said particular chromosome;

detecting non-radioactively any specifically hybridized clone or clones or
DNA fragments or oligo- or polynucleotides, and determining the number of copies
of said particular chromosome; and

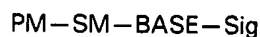
comparing said determined number of copies of said particular chromosome
with a number of copies of said particular chromosome determined for a normal cell

containing said particular chromosome, and determining whether the number of copies of said particular chromosome in said cell is abnormal.

1474. (Amended) A process for identifying a chromosome of interest in a cell containing other chromosomes, the process comprising the steps of:

providing a set of clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are specifically hybridizable to a locus or loci in said chromosome of interest, wherein said clones or fragments or said oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said non-radioactive modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula



wherein

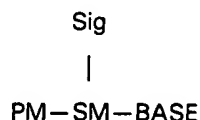
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a detectable non-radioactive moiety, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof, and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

- (ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

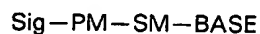
BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and

Sig is covalently attached SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and

Sig is covalently attached to PM directly or through a linkage group;

fixing the chromosomes from or in said cell;

contacting said fixed chromosomes under hybridizing conditions with said set of clones or DNA fragments or oligo- or polynucleotides, permitting specific hybridization of said set of clones or DNA fragments or oligo- or polynucleotides to said locus or loci in said chromosome of interest;

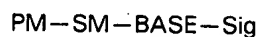
detecting non-radioactively any of said clones or DNA fragments or oligo- or polynucleotides which have specifically hybridized to said locus or loci in said chromosome of interest, and obtaining a pattern of hybridizations between said set of clones or DNA fragments or oligo- or polynucleotides and said chromosomes; and

identifying said chromosome of interest by means of said hybridization pattern obtained.

1475. (Amended) A process for identifying a plurality or all of the chromosomes in a cell of interest, the process comprising the steps of:

providing sets of clones or DNA fragments, or oligo- or polynucleotides derived from said clones, wherein said clones or fragments or said oligo- or polynucleotides are capable of hybridizing specifically to a locus or loci in a chromosome of said cell of interest, wherein each of said clones or DNA fragments or oligo- or polynucleotides in said sets are labeled with a different indicator molecule and each of said clones or DNA fragments or oligo- or polynucleotides comprises one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said detectable non-radioactive modified or labeled nucleotide or nucleotide analog are selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

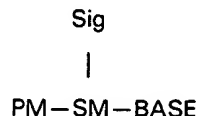
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine or a pyrimidine analog, at a position other than the C8 position when BASE is a purine or a purine analog, and at a position other than the C7 position when BASE is a 7-deazapurine or a 7-deazapurine analog thereof;

(ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

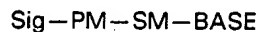
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and
Sig is covalently attached to PM directly or through a linkage group;

fixing the chromosomes from or in said cell;

contacting said fixed chromosomes under hybridizing conditions with said
sets of clones or DNA fragments or oligo- or polynucleotides, and permitting
specific hybridization of said sets of clones or DNA fragments or oligo- or
polynucleotides to the locus or loci in said chromosomes; and

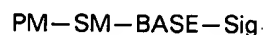
detecting non-radioactively any of said different indicator molecules in said
sets of clones or DNA fragments or oligo- or polynucleotides which have

specifically hybridized to the locus or loci in said chromosomes, and identifying any one of the chromosomes in said cell of interest.

1476. (Amended) A process for determining the number of chromosomes in an interphase cell of interest, the process comprising the steps of:

providing sets of clones or DNA fragments or oligo- or polynucleotides derived from said clones, wherein said set of clones or DNA fragments or oligo- or polynucleotides are specifically complementary to or specifically hybridizable with at least one locus or loci in a chromosome of said interphase cell of interest and each of said clones or DNA fragments or oligo- or polynucleotides in said sets comprises one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said detectable non-radioactive modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

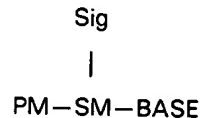
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety or a pyrimidine analog, at a position other than the C8 position when BASE is a purine or a purine analog, and at a position other than the C7 position when BASE is a 7-deazapurine or a 7-deazapurine analog;

- (ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

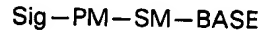
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached SM directly or through a linkage group; and

- (iii) a nucleotide or nucleotide analog, said nucleotide having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is detectable non-radioactive moiety,

wherein PM is covalently attached to the SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

contacting said interphase cell under hybridizing conditions with said sets of clones or DNA fragments or oligo- or polynucleotides, and permitting specific hybridization of said sets of clones or DNA fragments or oligo- or polynucleotides to any of the locus or loci in said chromosomes;

detecting non-radioactively any of said sets of clones or DNA fragments or oligo- or polynucleotides specifically hybridized to the locus or loci in said chromosomes, to obtain a pattern of generated signals; and comparing each

generated signal with other generated signals in said pattern, and determining the number of chromosomes in said interphase cell of interest.

-- 1477. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme. --

-- 1478. (NEW) The process according to claim 1477, wherein said enzyme comprises terminal transferase. --

-- 1479. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling. --

1480. (Wholly Rewritten) The process according to claim 1479, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.

-- 1481. (NEW) The process according to claim 1479, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase. --

-- 1482. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said incorporation comprises nick translation. --

-- 1483. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said incorporation is carried out by means of a polymerizing enzyme. --

-- 1484. (NEW) The process according to claim 1483, wherein said polymerizing enzyme comprises a polymerase. --

-- 1485. (NEW) The process according to claim 1484, wherein said polymerase is selected from the group consisting of DNA polymerase and RNA polymerase. --

- 1486. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a mono-phosphate, a di-phosphate, a tri-phosphate and a tetraphosphate. --
- 1487. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise nucleoside mono-, di- or tri-phosphate. --
- 1488. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said sugar moiety or sugar analog comprises a monosaccharide. --
- 1489. (NEW) The process according to claim 1488, wherein said monosaccharide comprises a furanose. --
- 1490. (NEW) The process according to claim 1489, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose. --
- 1491. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said base moiety or base analog BASE in any of said nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --
- 1492. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) is selected from the group consisting of a pyrimidine, a purine, a 7-deazapurine, and a combination of any of the foregoing. --

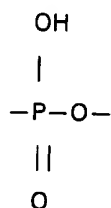
-- 1493. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position when BASE is a pyrimidine that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to BASE at a position when BASE is a purine that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof. --

-- 1494. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety in said nucleotide (i) is covalently attached to said BASE at a position selected from the group consisting of the N⁴ position when said pyrimidine comprises cytosine, the N² position when said purine comprises adenine or deazaadenine, the N⁶ position when said purine comprises guanine or deazaguanine, and combinations thereof. --

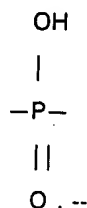
-- 1495. (NEW) The process according to claim 1489, wherein in said nucleotide (ii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 1496. (NEW) The process according to claim 1489, wherein in said nucleotide (iii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 1497. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



and



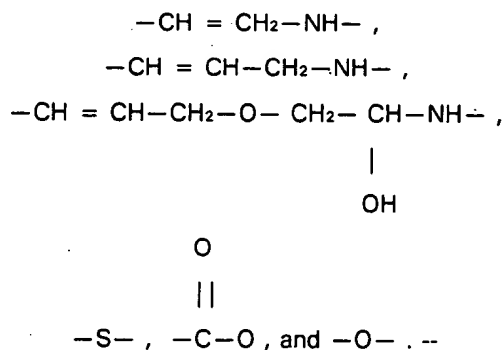
-- 1498. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein PM is a mono-, di or tri-phosphate, and wherein said nucleotide or nucleotide analog (iii), the Sig moiety is covalently attached to PM through a phosphorus or phosphate oxygen. --

1499. (Amended) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal.

-- 1500. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $-\text{CH}_2\text{NH}-$ moiety, or both. --

-- 1501. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group. --

-- 1502. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



-- 1503. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety. --

-- 1504. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein in any of said nucleotides or nucleotide analogs (i), (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group. --

-- 1505. (NEW) The process according to claim 1504, wherein said linkage group contains an amine. --

-- 1506. (NEW) The process according to claim 1505, wherein said amine comprises a primary amine. --

1507. (Amended) The process according to claim 1504, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

-- 1508. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises at least three carbon atoms. --

-- 1509. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --

-- 1510. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms. --

-- 1511. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms. --

-- 1512. (NEW) The process according to claim 1511, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent. --

-- 1513. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --

-- 1514. (NEW) The process according to claim 1513, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent. --

-- 1515. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide. --

-- 1516. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --

-- 1517. (NEW) The process according to claim 1516, wherein Sig comprises an electron dense component. --

-- 1518. (NEW) The process according to claim 1516, wherein said electron dense component comprises ferritin. --

-- 1519. (NEW) The process according to claim 1516, wherein Sig comprises a magnetic component. --

-- 1520. (NEW) The process according to claim 1519, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --

-- 1521. (NEW) The process according to claim 1519, wherein said magnetic component comprises magnetic beads. --

-- 1522. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises a sugar residue and the sugar residue is completed with or attached to a sugar binding protein or a polysaccharide binding protein. --

-- 1523. (NEW) The process according to claim 1522, wherein the binding protein comprises a lectin. --

-- 1524. (NEW) The process according to claim 1523, wherein the lectin comprises concanavalin A. --

-- 1525. (NEW) The process according to claim 1523, wherein said lectin is conjugated to ferritin. --

-- 1526. (NEW) The process according to claim 1516, wherein Sig comprises an enzyme. --

-- 1527. (NEW) The process according to claim 1526, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, galactosidase, ribonuclease, glucose oxidase and peroxidase, or a combination thereof. --

-- 1528. (NEW) The process according to claim 1516, wherein Sig comprises a hormone. --

-- 1529. (NEW) The process according to claim 1516, wherein Sig comprises a metal-containing component. --

-- 1530. (NEW) The process according to claim 1529, wherein said metal-containing component is catalytic. --

-- 1531. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule. --

-- 1532. (NEW) The process according to claim 1531, wherein said indicator molecule comprises an aromatic compound. --

-- 1533. (NEW) The process according to claim 1532, wherein said aromatic compound is heterocyclic. --

-- 1534. (NEW) The process according to claim 1533, wherein said heterocyclic aromatic compound is fluorescent. --

-- 1535. (NEW) The process according to claim 1534, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine, dansyl, and a combination of any of the foregoing. --

-- 1536. (NEW) The process according to claim 1535, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --

-- 1537. (NEW) The process according to claim 1516, wherein Sig comprises a fluorescent component. --

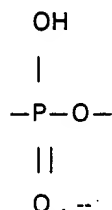
-- 1538. (NEW) The process according to claim 1537, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --

-- 1539. (NEW) The process according to claim 1538, wherein said fluorescent component comprises fluorescein. --

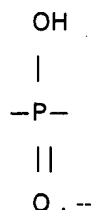
- 1540. (NEW) The process according to claim 1516, wherein Sig comprises a chemiluminescent component. --
- 1541. (NEW) The process according to claim 1516, wherein Sig comprises an antigenic or hapten component capable of completing with an antibody specific to the component. --
- 1542. (NEW) The process according to claim 1516, wherein Sig comprises an antibody component. --
- 1543. (NEW) The process according to claim 1516, wherein Sig comprises a chelating component. --
- 1544. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule. --
- 1545. (NEW) The process according to claim 1544, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, and a chelating component, or a combination of any of the foregoing. --
- 1546. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein any of nucleotide or nucleotide analogs (i), (ii) and (iii) are detectable by a means selected from the group consisting of a fluorescent measurement and a chemiluminescent measurement, or a combination thereof. --
- 1547. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig is detectable when the oligo- or polynucleotide is contained in a double-stranded ribonucleic or deoxyribonucleic acid duplex. --
- 1548. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig is detectable when it is attached to the nucleotide directly or through a linkage group. --

-- 1549. (NEW) The process according to claim 1548, wherein said linkage group does not interfere substantially with the characteristic ability of Sig to form a detectable signal. --

--1550. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig in said nucleotide (iii) is covalently attached to PM via the chemical linkage



-- 1551. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig in said nucleotide (iii) is covalently attached to PM via the chemical linkage



-- 1552. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein the oligo-or polynucleotide is terminally ligated or attached to a polypeptide. --

-- 1553. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, further comprising contacting the sample with a polypeptide capable of forming a complex with Sig and a moiety which can be detected when the complex is formed. --

-- 1554. (NEW) The process according to claim 1552, wherein the polypeptide comprises a polylysine. --

- 1555. (NEW) The process according to claim 1553, wherein the polypeptide comprises a polylysine. --
- 1556. (NEW) The process according to claim 1552, wherein the polypeptide comprises at least one member selected from the group consisting of avidin, streptavidin or anti-Sig immunoglobulin. --
- 1557. (NEW) The process according to claim 1553, wherein the polypeptide comprises at least one member selected from the group consisting of avidin, streptavidin or anti-Sig immunoglobulin. --
- 1558. (NEW) The process according to claim 1553, wherein Sig comprises a ligand and the polypeptide comprises an antibody thereto. --
- 1559. (NEW) The process according to claim 1553, wherein the moiety which can be detected when the complex is formed is selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --
- 1560. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said detecting step is carried out directly. --
- 1561. (NEW) The process according to claim 1560, wherein said direct detection is carried out on one or more indicator molecules. --
- 1562. (NEW) The process according to claim 1561, wherein said one or more indicator molecules comprise fluoresceinated nucleotides. --
- 1563. (NEW) The process according to claim 1562, wherein said fluoresceinated nucleotides or nucleotide analogs comprise fluoresceinated DNA. --
- 1564. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said detecting step is carried out by means of a directly detectable signal provided by said Sig detectable non-radioactive moiety. --

1565. (Amended) The process according to claim 1564, wherein said detecting step is carried out by means of a member selected from the group consisting of a fluorogenic compound, [a phosphorescent compound,] a chromogenic compound, a chemiluminescent compound and an electron dense compound.

1566. (Amended) The process according to claim 1564, wherein said detecting step the directly [-detectable] detectable non-radioactive signal is provided by an enzyme.

-- 1567. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said detecting step is carried out by means of an indirectly detectable signal provided by said Sig detectable non-radioactive moiety. --

-- 1568. (NEW) The process according to claim 1567, wherein said detecting step the indirectly detectable non-radioactive signal is provided by a member selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand and an enzyme. --

~~DELETED PER 2ND SUPPL. AMEND. 8/31/00 --1569. (NEW) The process according to claim 1567, wherein said detecting step the indirectly detectable non-radioactive signal is provided by a polynucleotide sequence capable of recognizing a signal containing moiety.~~

1570. (Twice Amended) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety is capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, [a phosphorescent measurement,] a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

-- 1571. (NEW) The process according to any of claims 1473, 1474, 1475 or 1476, further comprising one or more washing steps. --

1572. (Wholly Rewritten) The process according to claim 1473, 1474, 1475 or 1476, wherein said one or more clones or DNA fragments or oligo- or polynucleotides derived from clone or clones are derived from said particular chromosome or said chromosome of interest or said chromosome in said interphase cell of interest.

1573. (Amended) The process according to claim 1475, wherein each of [said.] said set of clones or DNA fragments or oligo- or polynucleotides is labeled with the same indicator molecule.

-- 1574. (NEW) The process according to any of claims. 1473, 1474 or 1475, wherein said detecting step is carried out by a means selected from the group consisting of manual means and automatic means. --

-- 1575. (NEW) The process according to claim 1574, wherein said manual means comprises visualization. --

-- 1576. (NEW) The process according to claim 1574, wherein said automatic means comprises computerized automatic karyotyping. --

-- 1577. (NEW) The process according to claim 1476, wherein each of said sets of clones or DNA fragments or oligo- or polynucleotides is labeled with the same indicator molecule. --

-- 1578. (NEW) The process according to claim 1476, wherein each of said sets of clones or DNA fragments or oligo- or polynucleotides is labeled with a different indicator molecule. --

-- 1579. (NEW) The process according to claim 1476, wherein said detecting and determining step is carried out by a means selected from the group consisting of manual means and automatic means. --

-- 1580. (NEW) The process according to claim 1579, wherein said manual means comprises visualization. --

-- 1581. (NEW) The process according to claim 1579, wherein said automatic means comprises computerized automatic karyotyping. --

1582. (Twice Amended) A process for preparing a detectable non-radioactively labeled oligo- or polynucleotide of interest, comprising the steps of:

(A) providing either:

(1) one or more detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA or an oligo- or polynucleotide of interest, alone or in conjunction with one or more other modified or unmodified nucleic acids selected from the group consisting of nucleotides, oligonucleotides and polynucleotides, wherein said other modified or unmodified nucleic acids are capable of incorporating into an oligo- or polynucleotide of interest, and wherein said detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs comprise one or more signaling moieties which are capable of providing directly or indirectly a detectable non-radioactive signal; or

(2) an oligo- or polynucleotide of interest comprising one or more said detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs, alone or in conjunction with one or more other modified or unmodified nucleic acids selected from the group consisting of nucleotides, oligonucleotides and polynucleotides;

wherein said detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate moiety, the base moiety or the base analog, and are selected from the group consisting of:

(i)

PM—SM—BASE—Sig

wherein

PM is a phosphate moiety or phosphate analog,

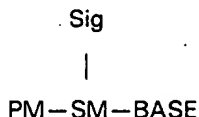
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a detectable non-radioactive moiety, and

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof, and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

(ii)



wherein

PM is a phosphate moiety or phosphate analog,

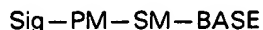
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a detectable non-radioactive moiety, and

wherein said PM is covalently attached to SM, said BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii)



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is detectable non-radioactive moiety; and

wherein PM is covalently attached to SM, BASE is covalently attached SM,
and Sig is covalently attached to PM directly or through a linkage group;
provided that when said nucleotide or nucleotide analog (iii) is attached to an
oligoribonucleotide or a polyribonucleotide, and provided that when Sig is attached
through a chemical linkage to a terminal PM at the 3' position of a terminal
ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal
oxidation of a 3' terminal ribonucleotide previously attached to said
oligoribonucleotide or polyribonucleotide; and

said oligo- or polynucleotide of interest; and

(B) either incorporating said one or more detectable non-radioactive chemically
modified or labeled nucleotides or nucleotide analogs (A)(1) into said oligo- or
polynucleotide, and preparing a non-radioactive labeled oligo- or polynucleotide of
interest, or preparing said oligo- or polynucleotide of interest from said oligo- or
polynucleotide recited in step (A)(2) above.

-- 1583. (NEW) The process according to claim 1582, wherein said oligo- or
polynucleotide of interest is derived from an organism. --

-- 1584. (NEW) The process according to claim 1583, wherein said organism is
living. --

-- 1585. (NEW) The process according to claims 1583 or 1584, wherein the
organism is selected from the group consisting of prokaryotes and eukaryotes. --

-- 1586. (NEW) The process according to claim 1585, wherein said organism
comprises a eukaryote. --

-- 1587. (NEW) The process according to claim 1586, wherein said eukaryotic
oligo- or polynucleotide of interest is contained within a chromosome. --

-- 1588. (NEW) The process according to claim 1586, wherein said eukaryote
comprises a mammal. --

- 1589. (NEW) The process according to claim 1588, wherein said mammalian oligo- or polynucleotide of interest is contained within a chromosome. --
- 1590. (NEW) The process according to claim 1588, wherein said mammal comprises a human being. --
- 1591. (NEW) The process according to claim 1590, wherein said human oligo- or polynucleotide of interest is contained within a chromosome. --
- 1592. (NEW) The process according to claim 1591, wherein said human chromosomal oligo- or polynucleotide of interest is part of a human gene library. --
- 1593. (NEW) The process according to claim 1592, wherein said living organism is selected from the group consisting of bacteria, fungi, viruses, yeast, mammals, and a combination of any of the foregoing. --
- 1594. (NEW) The process according to claim 1584, wherein said living organism comprises a mammal. --
- 1595. (NEW) The process according to claim 1594, wherein said mammal comprises a human being. --
- 1596. (NEW) The process according to claim 1582, wherein said incorporating step is carried out using an enzyme. --
- 1597. (NEW) The process according to claim 1596, wherein said enzyme comprises a polymerase. --
- 1598. (NEW) The process according to claim 1597, wherein said polymerase comprises DNA polymerase. --
- 1599. (NEW) The process according to claim 1582, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme. --
- 1600. (NEW) The process according to claim 1599, wherein said enzyme comprises terminal transferase. --

-- 1601. (NEW) The process according to claim 1582, wherein said nucleotide analog can be coupled to DNA or RNA by a coupling means selected from the group consisting of chemical coupling and enzymatic coupling. --

1602. (Wholly Rewritten) The process according to claim 1601, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide and formaldehyde.

-- 1603. (NEW) The process according to claim 1601, wherein said enzymatic coupling can be carried out by an enzymatic coupling means selected from the group consisting of DNA ligase and RNA ligase. --

-- 1604. (NEW) The process according to claim 1582, wherein said incorporation comprises nick translation. --

-- 1605. (NEW) The process according to claim 1582 or 1604, wherein said incorporation is carried out by means of a polymerizing enzyme. --

-- 1606. (NEW) The process according to claim 1605, wherein said polymerizing enzyme comprises a polymerase. --

-- 1607. (NEW) The process according to claim 1606, wherein said polymerase is selected from the group consisting of DNA polymerase and RNA polymerase. --

1608. (Amended) The process according to claim 1582, wherein said one or more detectable non-radioactive chemically modified nucleotides or said other modified or unmodified nucleic acids comprise a nucleoside di- or tri-phosphate.

-- 1609. (NEW) The process according to claim 1582, wherein said incorporating step is template dependent or template independent. --

-- 1610. (NEW) The process according to claim 1609, wherein said incorporating step is template dependent. --

1611. (Wholly Rewritten) The process according to claim 1582, wherein said labeled oligo- or polynucleotide of interest prepared by said incorporating step comprises at least one internal modified nucleotide.

-- 1612. (NEW) The process according to claim 1582, wherein said labeled oligo- or polynucleotide of interest prepared by said incorporating step comprises at least one terminal modified nucleotide. --

~~DELETED PER 2ND SUPPL. AMEND. 8/31/00 -- 1613. (NEW) The process according to claim 1582, wherein said labeled oligo- or polynucleotide prepared by said incorporating step comprises at least one internal modified nucleotide and at least one terminal modified nucleotide. --~~

-- 1614. (NEW) The process according to claim 1582, wherein said phosphate moiety or phosphate analog is selected from the group consisting of a monophosphate, a di-phosphate, a tri-phosphate and a tetra-phosphate. --

-- 1615. (NEW) The process according to claim 1582, wherein any of said nucleotides or nucleotide analogs (i), (ii) or (iii) comprise a nucleoside mono-, di- or tri-phosphate. --

-- 1616. (NEW) The process according to claim 1582, wherein said sugar moiety or sugar analog comprises a monosaccharide. --

-- 1617. (NEW) The process according to claim 1616, wherein said monosaccharide comprises a furanose. --

-- 1618. (NEW) The process according to claim 1617, wherein said furanose is selected from the group consisting of ribose, deoxyribose and dideoxyribose. --

-- 1619. (NEW) The process according to claim 1582, wherein in said chemically modified nucleotides or nucleotide analogs (i) Sig is covalently attached to said BASE at a position when BASE is a pyrimidine or pyrimidine analog that is selected from the group consisting of the C2 position, the N3 position, the C6 position, and combinations thereof, or is covalently attached to BASE at a position when BASE is a purine or purine analog that is selected from the group consisting of the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, and combinations thereof. --

-- 1620. (NEW) The process according to claim 1582, wherein in said chemically modified nucleotides or nucleotide analogs (i) Sig is covalently attached to said BASE at a position selected from the group consisting of the N⁴ position when said pyrimidine or pyrimidine analog comprises cytosine or a cytosine analog, the N² position when said purine or purine analog comprises adenine, an adenine analog, or deazaadenine, the N⁶ position when said purine comprises guanine or deazaguanine, and combinations thereof. --

-- 1621. (NEW) The process according to claim 1582, wherein said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) or both is selected from the group consisting of a pyrimidine, a pyrimidine analog, a purine, a purine analog, a 7-deazapurine, a 7-deazapurine analog, and a combination of any of the foregoing. --

-- 1622. (NEW) The process according to claim 1582, wherein said sugar moiety or sugar analog SM comprises a monosaccharide or a furanose, and said base moiety or base analog BASE in nucleotides (i), (ii) or (iii) or both is selected from the group consisting of a pyrimidine, a pyrimidine analog, a purine, a purine analog, a 7-deazapurine, a 7-deazapurine analog, and a combination of any of the foregoing. --

-- 1623. (NEW) The process according to claim 1582, wherein in said incorporating step, Sig in the nucleotide (i) is covalently attached to BASE through a linkage group. --

1624. (Amended) The process according to claim 1623, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

-- 1625. (NEW) The process according to claim 1623, wherein said linkage group contains an amine. --

-- 1626. (NEW) The process according to claim 1625, wherein said amine comprises a primary amine. --

-- 1627. (NEW) The process according to claim 1582, wherein in said incorporating step, Sig in the nucleotide (ii) is covalently attached to SM through a linkage group. --

1628. (Amended) The process according to claim 1627, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

-- 1629. (NEW) The process according to claim 1627, wherein said linkage group contains an amine. --

-- 1630. (NEW) The process according to claim 1629, wherein said amine comprises a primary amine. --

-- 1631. (NEW) The process according to claim 1582, wherein in said incorporating step, Sig in the nucleotide (iii) is covalently attached to PM through a linkage group. --

1632. (Amended) The process according to claim 1631, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

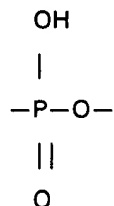
-- 1633. (NEW) The process according to claim 1631, wherein said linkage group contains an amine. --

-- 1634. (NEW) The process according to claim 1633, wherein said amine comprises a primary amine. --

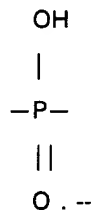
-- 1635. (NEW) The process according to claim 1617, wherein in said nucleotide (ii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or a pyrimidine analog, or the N9 position when BASE is a purine, a purine analog, 7-deazapurine, or a 7-deazapurine analog, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 1636. (NEW) The process according to claim 1617, wherein in said nucleotide (iii), PM is attached to said furanose at a position independently selected from the group consisting of the 2', 3', and 5' positions, or any combination thereof, and BASE is attached to the 1' position of said furanose from the N1 position when BASE is a pyrimidine or a pyrimidine analog, or the N9 position when BASE is a purine, a purine analog, 7-deazapurine, or a 7-deazapurine analog, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization. --

-- 1637. (NEW) The process according to claim 1582, wherein said covalent attachment in nucleotide or nucleotide analog (iii) is selected from the group consisting of



and



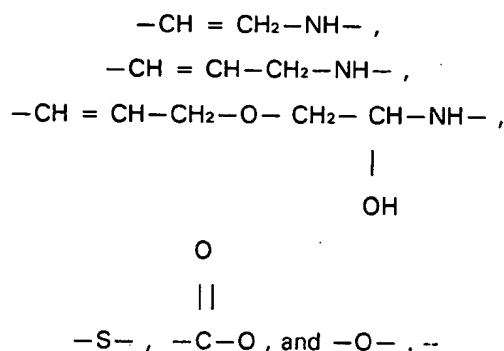
-- 1638. (NEW) The process according to claim 1582, wherein PM is a mono-, di or tri-phosphate, and wherein in said nucleotide or nucleotide analog (iii), the Sig moiety is covalently attached to PM through a phosphorus or phosphate oxygen. --

1639. (Amended) The process according to claim 1582, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal.

-- 1640. (NEW) The process according to claim 1582, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $\text{--CH}_2\text{NH--}$ moiety, or both. --

-- 1641. (NEW) The process according to claim 1582, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises an allylamine group. --

-- 1642. (NEW) The process according to claim 1582, wherein said covalent attachment in any of nucleotides (i), (ii) or (iii) comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



--1643. (NEW) The process according to claim 1582, wherein said covalent attachment in any of nucleotides or nucleotide analogs (i), (ii) or (iii) includes a glycosidic linkage moiety. --

-- 1644. (NEW) The process according to claim 1582, wherein in said nucleotides or nucleotide analogs (i), (ii) or (iii), Sig is covalently attached to BASE, SM or PM through a linkage group. --

-- 1645. (NEW) The process according to claim 1644, wherein said linkage group contains an amine. --

--1646. (NEW) The process according to claim 1645, wherein said amine comprises a primary amine. --

1647. (Amended) The process according to claim 1645, wherein said linkage group does not substantially interfere with formation of the signaling moiety or detection of the detectable non-radioactive signal.

-- 1648. (NEW) The process according to claim 1582, wherein said Sig comprises at least three carbon atoms. --

-- 1649. (NEW) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond. --

-- 1650. (NEW) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms. --

-- 1651. (NEW) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms. --

-- 1652. (NEW) The process according to claim 1651, wherein said heterocyclic aromatic compound is fluorescent. --

-- 1653. (NEW) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms. --

-- 1654. (NEW) The process according to claim 1653, wherein said heterocyclic aromatic compound is fluorescent. --

-- 1655. (NEW) The process according to claim 1582, wherein said Sig comprises a monosaccharide, polysaccharide or an oligosaccharide. --

-- 1656. (NEW) The process according to claim 1582, wherein said Sig comprises a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --

-- 1657. (NEW) The process according to claim 1656, wherein said Sig comprises an electron dense component. --

-- 1658. (NEW) The process according to claim 1657, wherein said electron dense component comprises ferritin. --

-- 1659. (NEW) The process according to claim 1656, wherein said Sig comprises a magnetic component. --

-- 1660. (NEW) The process according to claim 1659, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide. --

-- 1661. (NEW) The process according to claim 1659, wherein said magnetic component comprises magnetic beads. --

-- 1662. (NEW) The process according to claim 1582, wherein said Sig comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein. --

-- 1663. (NEW) The process according to claim 1662, wherein the binding protein comprises a lectin. --

-- 1664. (NEW) The process according to claim 1663, wherein the lectin comprises concanavalin A. --

-- 1665. (NEW) The process according to claim 1663, wherein said lectin is conjugated to ferritin. --

-- 1666. (NEW) The process according to claim 1656, wherein said Sig comprises an enzyme. --

-- 1667. (NEW) The process according to claim 1666, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, galactosidase, ribonuclease, glucose oxidase and peroxidase, or a combination thereof. --

-- 1668. (NEW) The process according to claim 1656, wherein said Sig comprises a hormone. --

-- 1669. (NEW) The process according to claim 1656, wherein said Sig comprises a metal-containing component. --

-- 1670. (NEW) The process according to claim 1669, wherein said metal-containing component is catalytic. --

-- 1671. (NEW) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety comprises an indicator molecule. --

-- 1672. (NEW) The process according to claim 1671, wherein said indicator molecule comprises an aromatic compound. --

-- 1673. (NEW) The process according to claim 1672, wherein said aromatic compound is heterocyclic. --

-- 1674. (NEW) The process according to claim 1673, wherein said heterocyclic aromatic compound is fluorescent. --

-- 1675. (NEW) The process according to claim 1674, wherein the fluorescent heterocyclic aromatic compound is selected from the group consisting of fluorescein, rhodamine and dansyl. --

-- 1676. (NEW) The process according to claim 1675, wherein said fluorescent heterocyclic aromatic compound comprises fluorescein. --

-- 1677. (NEW) The process according to claim 1671, wherein said indicator molecule comprises a member selected from the group consisting of a fluorescent component, a chemiluminescent component, and a chelating component, or a combination of any of the foregoing. --

-- 1678. (NEW) The process according to claim 1656, wherein said Sig comprises a fluorescent component. --

-- 1679. (NEW) The process according to claim 1678, wherein said fluorescent component is selected from the group consisting of fluorescein, rhodamine and dansyl. --

-- 1680. (NEW) The process according to claim 1679, wherein said fluorescent component comprises fluorescein. --

-- 1681. (NEW) The process according to claim 1656, wherein said Sig comprises a chemiluminescent component. --

-- 1682. (NEW) The process according to claim 1656, wherein said Sig comprises an antigenic or hapten component capable of completing with an antibody specific to the component. --

-- 1683. (NEW) The process according to claim 1656, wherein said Sig comprises an antibody component. --

-- 1684. (NEW) The process according to claim 1656, wherein said Sig comprises a chelating component. --

-- 1685. (NEW) The process according to claim 1582, wherein any of nucleotide or nucleotide analogs (i), (ii) and (iii) are detectable by a means selected from the group consisting of a fluorescent measurement and a chemiluminescent measurement, or a combination thereof. --

1686. (Amended) The process according to claim 1582, wherein said Sig is detectable non-radioactively when the oligo- or polynucleotide is contained in a double-stranded ribonucleic or deoxyribonucleic acid duplex.

1687. (Amended) The process according to claim 1582, wherein said Sig is detectable non-radioactively when it is attached to the nucleotide directly or through a linkage group.

1688. (Amended) The process according to claim 1687, wherein said linkage group does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal.

1689. (Wholly Rewritten) The process according to claim 1582, wherein said labeled oligo- or polynucleotide of interest is terminally ligated or attached to a polypeptide.

-- 1690. (NEW) The process according to claim 1689, further comprising contacting the sample with a polypeptide capable of forming a complex with Sig and a moiety which can be detected when the complex is formed. --

-- 1691. (NEW) The process according to claim 1689, wherein the polypeptide comprises a polylysine. --

-- 1692. (NEW) The process according to claim 1689, wherein the polypeptide comprises at least one member selected from the group consisting of avidin, streptavidin or anti-Sig immunoglobulin. --

1693. (Amended) The process according to claim 1690, wherein said Sig comprises a ligand [and.] and the polypeptide comprises an antibody thereto.

-- 1694. (NEW) The process according to claim 1690, wherein the moiety which can be detected when the complex is formed is selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --

-- 1695. (NEW) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety is capable of being directly detected. --

1696. (Amended) The process according to claim 1695, wherein said directly detectable signal providing Sig detectable non-radioactive moiety is selected from the group consisting of a fluorogenic compound, [a phosphorescent compound,] a chromogenic compound, a chemiluminescent compound, an electron dense compound and an enzyme.

-- 1697. (NEW) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety is capable of being indirectly detected. --

1698. (Wholly Rewritten) The process according to claim 1697, wherein said detecting step the indirectly detectable signal is provided by a member selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme and a combination of any of the foregoing.

1699. (Twice Amended) The process according to claim 1582, wherein said Sig detectable non-radioactive moiety is capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, [a phosphorescent measurement,] a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

1700. (Amended) A process for determining the sequence of a nucleic acid of interest, comprising the steps of:

providing or generating non-radioactive labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, wherein said detectable non-radioactive modified or labeled nucleotides or nucleotide analogs comprise one or more chelating compounds or chelating components capable of chelating a radioactive metal and providing a detectable radioactive signal, and wherein said one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety, or the base analog thereof;

subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments; and

detecting the presence of each of said separated or resolved fragments by means of the detectable radioactive signal provided by a radioactive metal chelated by said chelating compounds or chelating components in the detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, and determining the sequence of said nucleic acid of interest.

1701. (Twice Amended) A process for determining the sequence of a nucleic acid of interest, comprising the steps of:

providing or generating detectable non-radioactive labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, wherein said detectable non-radioactive modified or labeled nucleotides or nucleotide analogs comprise one or more chelating compounds or chelating components capable of chelating a radioactive metal and providing a detectable radioactive signal, and wherein said one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety, or the base analog thereof;

introducing or subjecting said fragments to a sequencing gel;

separating or resolving said fragments in said sequencing gel; and

detecting each of the separated or resolved fragments by means of the detectable radioactive signal provided by a radioactive metal chelated by said chelating compounds or chelating components in the detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, and determining the sequence of said nucleic acid of interest.

1702. (Twice Amended) A process for determining the sequence of a nucleic acid of interest, comprising the steps of:

providing or generating detectable non-radioactive labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, wherein said detectable non-radioactive modified or labeled nucleotides or nucleotide analogs comprise one or more chelating compounds or chelating components capable of chelating a radioactive metal and providing a detectable radioactive signal, and wherein said one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety or the base analog thereof;

radioactively detecting with a sequencing gel the detectable non-radioactive labeled nucleic acid fragments [with a sequencing gel] by means of a radioactive metal chelated by said chelating compounds or chelating components; and
determining the sequence of said nucleic acid of interest.

1703. (Twice Amended) A process for determining the sequence of a nucleic acid of interest, comprising the step of detecting with a sequencing gel one or more detectable non-radioactive labeled nucleic acid fragments comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, wherein said detectable non-radioactive modified or labeled nucleotides or nucleotide analogs comprise one or more chelating compounds or chelating components capable of chelating a radioactive metal and providing a detectable radioactive signal, and wherein said one or more detectable non-radioactive modified nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the base moiety or the base analog thereof.

1704. (Twice Amended) A process for determining in a sequencing gel the presence of nucleic acid fragments comprising a sequence complementary to a nucleic acid sequence of interest or a portion thereof, said process comprising the steps of:

(A) providing

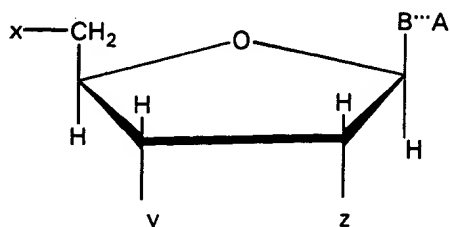
(i) one or more detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into a nucleic acid, or

(ii) one or more oligonucleotides or polynucleotides comprising at least one of said detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs; or

(iii) both (i) and (ii);

wherein said detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs (i) and said oligonucleotides and polynucleotides (ii) are capable of attaching to or coupling to or incorporating into or forming one or more nucleic acid fragments, wherein said detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs comprise one or more chelating compounds or chelating components capable of chelating a radioactive metal and providing a detectable radioactive signal, and wherein said detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs have been modified non-disruptively or disruptively on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety or the base analog thereof; and;

(B) incorporating said one or more detectable non-radioactive chemically modified or labeled nucleotides or nucleotide analogs (i) or said one or more oligonucleotides or polynucleotides comprising at least one of said detectable non-radioactive chemically modified or labeled nucleotides (ii), or both (i) and (ii), into said one or more nucleic acid fragments, to prepare detectable non-radioactive labeled fragments, each such fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, said detectable non-radioactive labeled fragments further comprising one or more detectable non-radioactive chemically modified nucleotides or nucleotide analogs selected from the group consisting of:

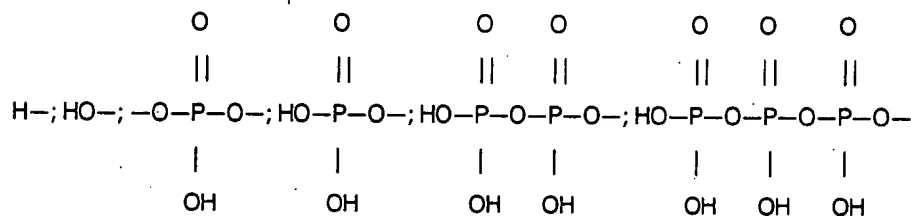


wherein B represents a purine moiety, a 7-deazapurine moiety, a pyrimidine moiety, or an analog of any of the foregoing, and B is covalently bonded to the C1'-position of the sugar moiety or sugar analog, provided that whenever B is a purine, a purine analog, a 7-deazapurine moiety or a 7-deazapurine analog, the sugar moiety or sugar analog is attached at the N9 position of the purine moiety, the purine analog, the, 7-deazapurine moiety or the 7-analog thereof, and whenever B is a pyrimidine moiety or a pyrimidine analog, the sugar moiety or sugar analog is attached at the N1 position of the pyrimidine moiety or the pyrimidine analog;

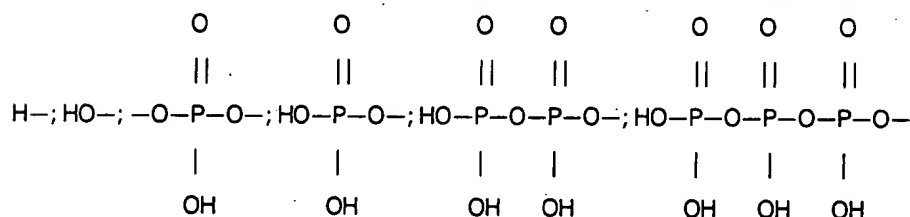
wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety comprising a chelating compound or chelating component capable of chelating a radioactive metal and providing directly or indirectly a detectable radioactive signal; and

wherein B and A are covalently attached directly or through a linkage group, and

wherein x comprises a member selected from the group consisting of:

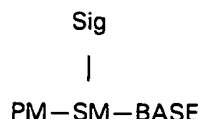


wherein y comprises a member selected from the group consisting of:



wherein z comprises a member selected from the group consisting of
 H- and HO- [--]

(ii)



wherein

PM is a phosphate moiety or phosphate analog,

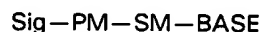
SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a radioactive metal and providing a detectable radioactive signal, and

wherein said PM is covalently attached to SM, said BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii)



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog,

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a radioactive metal and providing a detectable radioactive signal; and

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

(C) transferring or subjecting said labeled fragments to a sequencing gel;

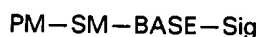
(D) separating or resolving said labeled fragments; and

(E) detecting directly or indirectly the presence of said labeled fragments by means of a radioactive metal chelated by said chelating compounds or chelating components.

1705. (Amended) A process for detecting a nucleic acid of interest in a sample, which process comprises the steps of:

(a) specifically hybridizing said nucleic acid of interest in the sample with one or more oligo- or polynucleotides, each such oligo- or polynucleotide being complementary to or capable of hybridizing with said nucleic acid of interest or a portion thereof, wherein said oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said detectable non-radioactive modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

(i) a nucleotide or nucleotide analog having the formula



wherein

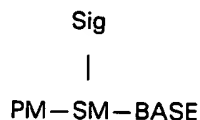
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety or a base analog of any of the foregoing; and

Sig is a signaling moiety comprising a chelating compound or component capable of chelating a radioactive metal and providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof, and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization;

(ii) a nucleotide or nucleotide analog having the formula



wherein

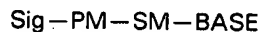
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or component capable of providing chelating a radioactive metal and a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization; and

(iii) a nucleotide or nucleotide analog, said nucleotide having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or components capable of chelating a radioactive metal and providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group, and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization;

provided that when said nucleotide or nucleotide analog (iii) is attached to an oligoribonucleotide or a polyribonucleotide, and provided that when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal

oxidation of a 3' terminal ribonucleotide previously attached to said
oligoribonucleotide or polyribonucleotide; and

(b) detecting radioactively the presence of said signaling moieties Sig in any of
the oligo- or polynucleotides which have hybridized to said nucleic acid of
interest by means of a radioactive metal chelated by said chelating compounds or
chelating components.

1706. (Amended) A process for detecting a nucleic acid of interest in a sample,
which process comprises the steps of:

(A) providing:

(i) an oligo- or polynucleotide having two segments:

(a) a first segment complementary to and capable of
hybridizing to a portion of said nucleic acid of interest; and

(b) a second segment comprising at least one protein binding
sequence; and

(ii) a detectable protein capable of binding to said protein binding
sequence and comprising a chelating compound or chelating
component capable of chelating a radioactive metal and providing a
detectable radioactive signal;

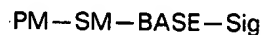
(B) contacting a sample suspected of containing said nucleic acid of
interest with said oligo- or polynucleotide [(ii)] (i) and said detectable protein [(iii)]
(ii) to form a complex;

(C) detecting radioactively the presence of said protein in said complex
and said nucleic acid of interest by means of a radioactive metal chelated by said
chelating compound or chelating component.

1707. (Twice Amended) A process for determining whether the number of copies of a particular chromosome in a cell is normal or abnormal, the process comprising the steps of:

contacting said cell under hybridizing conditions with one or more clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are capable of hybridizing specifically to a locus or loci of said particular chromosome or a portion thereof; wherein said clones or fragments or oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said detectable non-radioactive modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula



wherein

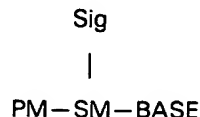
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety or an analog of any of the foregoing thereof, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a radioactive metal and providing a detectable radioactive signal, wherein PM is covalently attached to the SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof, and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

(ii) a nucleotide or nucleotide analog having the formula



wherein

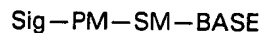
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a radioactive metal and providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a radioactive metal and providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group, to permit specific hybridization of said clone or clones or DNA fragments or oligo- or polynucleotides to the locus or loci of said particular chromosome;

detecting radioactively the signal generated by said specifically hybridized clone or clones or DNA fragments or oligo- or polynucleotides by means of a radioactive metal chelated by said chelating compound or chelating component, and determining the number of copies of said particular chromosome; and

comparing said determined number of copies of said particular chromosome with a number of copies of said particular chromosome determined for a normal cell containing said particular chromosome, and determining whether the number of copies of said particular chromosome in said cell is abnormal.

1708. (Amended) A process for identifying a chromosome of interest in a cell containing other chromosomes, the process comprising the steps of:

providing a set of clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are specifically hybridizable to a locus or loci in said chromosome of interest, wherein said clones or fragments or oligo- or polynucleotides comprise one or more detectable modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula



wherein

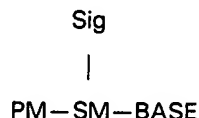
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a radioactive metal and providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof, and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

(ii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a radioactive metal and providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a radioactive metal and providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

fixing the chromosomes from or in said cell;

contacting said fixed chromosomes under hybridizing conditions with said set of clones or DNA fragments or oligo- or polynucleotides, permitting specific hybridization of said set of clones or DNA fragments or oligo- or polynucleotides to said locus or loci in said chromosome of interest;

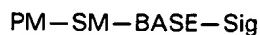
detecting radioactively by means of a radioactive metal chelated by said chelating compound or chelating component any signal generated by each of said clones or DNA fragments or oligo- or polynucleotides which have specifically hybridized to said locus or loci in said chromosome of interest, and obtaining a pattern of hybridizations between said set of clones or DNA fragments or oligo- or polynucleotides and said chromosomes; and

identifying said chromosome of interest by means of said hybridization pattern obtained.

1709. (Amended) A process for identifying a plurality or all of the chromosomes in a cell of interest, the process comprising the steps of:

providing sets of clones or DNA fragments, or oligo- or polynucleotides derived from said clones, wherein each of said set of clones or DNA fragments or oligo- or polynucleotides are specifically hybridizable to a locus or loci in a chromosome of said cell of interest, wherein each of said clones or DNA fragments or oligo- or polynucleotides in said sets are labeled with a different indicator molecule and each of said clones or DNA fragments or oligo- or polynucleotides comprise one or more detectable modified or labeled nucleotides or nucleotide analogs capable of detection, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotide or nucleotide analogs are selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

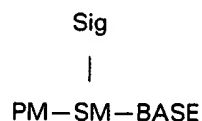
SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a radioactive metal and providing a detectable

radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine or a pyrimidine analog, at a position other than the C8 position when BASE is a purine or a purine analog, and at a position other than the C7 position when BASE is a 7-deazapurine or a 7-deazapurine analog thereof;

(ii) a nucleotide or nucleotide analog having the formula



wherein

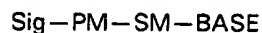
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a radioactive metal and providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a radioactive metal and providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

fixing the chromosomes from or in said cell;

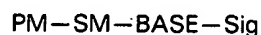
contacting said fixed chromosomes under hybridizing conditions with said sets of clones or DNA fragments or oligo- or polynucleotides, and permitting specific hybridization of said sets of clones or DNA fragments or oligo- or polynucleotides to the locus or loci in said chromosomes; and

detecting radioactively by means of a radioactive metal chelated by said chelating compound or chelating component any signal generated by each of said different indicator molecules in said sets of clones or DNA fragments or oligo- or polynucleotides which have specifically hybridized to the locus or loci in said chromosomes, and identifying any one of the chromosomes in said cell of interest.

1710. (Amended) A process for determining the number of chromosomes in an interphase cell of interest, the process comprising the steps of:

providing sets of clones or DNA fragments, or oligo- or polynucleotides derived from said clones, wherein each of said set of clones or DNA fragments or oligo- or polynucleotides are specifically complementary to or specifically hybridizable with at least one locus or loci in a chromosome of said interphase cell of interest, wherein each of said clones or DNA fragments or oligo- or polynucleotides in said sets comprise one or more detectable modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotide or nucleotide analog are selected from the group consisting of:

- (i) a nucleotide or nucleotide analog having the formula



wherein

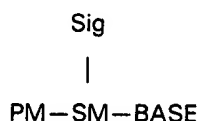
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a radioactive metal and providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety or a pyrimidine analog, at a position other than the C8 position when BASE is a purine or a purine analog, and at a position other than the C7 position when BASE is a 7-deazapurine or a 7-deazapurine analog;

- (ii) a nucleotide or nucleotide analog having the formula



wherein

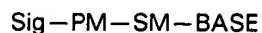
PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a radioactive metal and providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached SM directly or through a linkage group; and

- (iii) a nucleotide or nucleotide analog, said nucleotide having the formula



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a radioactive metal and providing a detectable radioactive signal, wherein PM is covalently attached to the SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

contacting said interphase cell under hybridizing conditions with said sets of clones or DNA fragments or oligo- or polynucleotides, and permitting specific hybridization of said sets of clones or DNA fragments or oligo- or polynucleotides to any of the locus or loci in said chromosomes;

detecting radioactively by means of a radioactive metal chelated by said chelating compound or chelating component any signals generated by each of said sets of clones or DNA fragments or oligo- or polynucleotides specifically hybridized to the locus or loci in said chromosomes, to obtain a pattern of generated signals; and comparing each generated signal with other generate signals in said pattern, and determining the number of chromosomes in said interphase cell of interest.

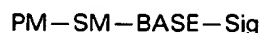
1711. (Amended) A process for preparing a labeled oligo- or polynucleotide of interest, comprising the steps of:

(A) providing either:

(1) one or more detectable chemically modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA or an oligo- or polynucleotide of interest, alone or in conjunction with one or more other modified or unmodified nucleic acids selected from the group consisting of nucleotides, oligonucleotides and polynucleotides, wherein said other modified or unmodified nucleic acids are capable of incorporating into an oligo- or polynucleotide of interest, and wherein said chemically modified or labeled nucleotides or nucleotide analogs comprise one or more signaling moieties comprising a chelating compound or chelating component capable of chelating a radioactive metal and providing a detectable radioactive signal, or

(2) an oligo- or polynucleotide of interest comprising one or more of said detectable chemically modified or labeled nucleotides or nucleotide analogs, alone or in conjunction with one or more other modified or unmodified nucleic acids selected from the group consisting of nucleotides, oligonucleotides and polynucleotides, wherein said chemically modified or labeled nucleotides or nucleotide analogs are modified on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate moiety, the base moiety or the base analog, and are selected from the group consisting of:

(i)



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a radioactive metal and providing a detectable radioactive signal, and

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof, and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

(ii)

Sig

|



wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a radioactive metal and providing a radioactive signal, and wherein said PM is covalently attached to SM, said BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii)

Sig—PM—SM—BASE

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, or a base analog of any of the foregoing, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of chelating a radioactive metal and providing a detectable radioactive signal; and wherein PM is covalently attached to SM, BASE is covalently attached SM, and Sig is covalently attached to PM directly or through a linkage group, provided that when said nucleotide or nucleotide analog (iii) is attached to an oligoribonucleotide or a polyribonucleotide, and provided that when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide; and said oligo- or polynucleotide of interest;

and

(B) either incorporating said one or more modified or labeled nucleotides or nucleotide analogs (A)(1) into said oligo- or polynucleotide, and preparing a labeled oligo- or polynucleotide of interest, or preparing said oligo- or polynucleotide of interest from said oligo- or polynucleotide recited in step (A)(2) above.

1712. (Amended) A process for detecting the presence of a nucleic acid of interest in a sample, comprising the steps of:

providing or generating (i) one or more detectable non-radioactively labeled oligonucleotides or polynucleotides, each of said detectable non-radioactively labeled oligonucleotides or polynucleotides comprising a sequence sufficiently complementary to said nucleic acid of interest or to a portion thereof to specifically hybridize [thereto] therewith, wherein said one or more detectable non-radioactively labeled oligonucleotides or polynucleotides comprise one or more detectable non-radioactively modified or labeled nucleotides or nucleotide analogues, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said detectable non-radioactively modified or labeled nucleotides or nucleotide analogs have been modified or labeled on at least one of the sugar moiety, the sugar analog, the phosphate moiety, the phosphate analog, the base moiety, or the base analog thereof, and (ii) a sample that may contain said nucleic acid of interest;

forming in liquid phase hybrids comprising said one or more detectable non-radioactively labeled oligonucleotides or polynucleotides [and] specifically hybridized with said nucleic acid of interest;

separating or resolving in a gel said formed hybrids; and

detecting non-radioactively the separated or resolved hybrids to detect the presence of said nucleic acid of interest.

-- 1713. (NEW) The process according to claim 1712, wherein after said hybrid forming step, the liquid phase is subjected to nuclease treatment. --

-- 1714. (NEW) The process according to claim 1712, wherein said nucleic acid of interest is selected from the group consisting of DNA, RNA and DNA-RNA. --

-- 1715. (NEW) The process according to claim 1712, wherein said one or more detectable oligonucleotides or polynucleotides are selected from the group consisting of DNA, RNA and DNA-RNA. --

-- 1716. (NEW) The process according to claim 1712, wherein said one or more detectable oligonucleotides or polynucleotides comprise a member selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component and a chelating component. --

-- 1717. (NEW) The process according to claim 1712, wherein said non-radioactive detection step is carried out directly or indirectly. --

1718. (Wholly Rewritten) The process according to claim 1712, wherein said detecting step is carried out by means of a member selected from the group consisting of enzymatic measurement, a fluorescent measurement, a phosphorescent measurement, a chemiluminescent measurement, a microscopic measurement and an electron density measurement.

-- 1719. (NEW) The process according to claim 569, wherein said nucleic acid of interest is selected from the group consisting of DNA, RNA and DNA-RNA. --

-- 1720. (NEW) The process according to claim 721, wherein said nucleic acid of interest is selected from the group consisting of DNA, RNA and DNA-RNA. --

-- 1721. (NEW) The process according to claim 873, wherein said nucleic acid of interest is selected from the group consisting of DNA, RNA and DNA-RNA. --

-- 1722. (NEW) The process according to claim 1025, wherein said nucleic acid of interest is selected from the group consisting of DNA, RNA and DNA-RNA. --

-- 1723. (NEW) The process according to any of claims 710, 862, 1014 or 1166, wherein said direct detection is carried out with the same indicator molecules. --

-- 1724. (NEW) The process according to any of claims 710, 862, 1014 or 1166, wherein said direct detection is carried out with different indicator molecules. --

-- 1725. (NEW) The process according to claim 1400, wherein said direction detection is carried out with the same indicator molecules. --

-- 1726. (NEW) The process according to claim 1400, wherein said direction
detection is carried out with different indicator molecules. --

-- 1727. (NEW) The process according to claim 1712, wherein said detecting step
comprises localizing said separated or resolved hybrids. --

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